HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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ADULT SPEAKER PRESENTATIONS

Sp01

Induction therapy choices and responses in a third world country: A single center study from Pakistan

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A B S T R A C T

Background: Leukaemia accounts for approximately 2.5% of all new cancer incidence and 3.1% of cancer-related mortality with a significant number of the total presenting as Acute Lymphocytic Leukemia. Acute Lymphocytic Leukemia (ALL) poses a healthcare burden in the majority of the countries of the world but is more so a case in resource-limited countries where access to comprehensive healthcare is often limited and scarcely available. This article tries to highlight the challenges in ALL treatments in one such region by presenting the facts regarding treatments employed and patient outcomes seen.
Method: This was a retrospective single-institution study in a tertiary care setup examining Ph neg ALL patient data from Jan 2019 to Dec 2020. It was stratified according to various parameters ranging from presentation to mode of diagnosis as well as treatment strategies and responses achieved after induction including mortality. Conventional chemotherapy regimens for ALL treatment were used with corticosteroids, vincristine, anthracyclines, asparaginase, cytosar, and MTX being the backbone of ALL induction. Cytogenetics were not possible due to resource constraints.
Results: Data showed 85 patients being managed during the mentioned time period. 65 percent were males and 68 percent were between the age 15 to 30 years. Approximately 80 percent had no co-morbid condition including diabetes, hypertension, ischemic heart disease or Hep B/C positivity. Around 60 percent were diagnosed on immunophenotyping by flowcytometry and 62 percent used HyperCVAD as the induction protocol. Patients who achieved CR were 62 percent after single induction and most were assessed after count recovery on (3-4 weeks) or after 6 weeks with the percentages being 32 and 41 respectively. Duration of admission was for 1-3 weeks for almost 70 percent of the patients and those alive at the end of induction were around 90 percent.
Conclusion: In conclusion, the treatment of Acute Lymphocytic Leukemia in resource-limited countries remains a formidable task,sometimes requiring innovative and sustainable approaches. Due to limited resources, a resource stratified rather than risk-stratified treatment approach is often utilized to tailor therapy. This approach ensures that relatively better resourced patients receive more intensive treatment others are spared unnecessary toxicity. While the challenges in resource-limited settings are significant, the treatment strategies and chemotherapy protocols, if modified as per need and implemented effectively, hold promise in improving outcomes for patients with Ph negative Acute Lymphocytic Leukemia in regions which have limited resources at their disposal.

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Sp02

Bone marrow transplantation versus chimeric antigen receptor T cells (CAR-T) therapy for hematological malignancies

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Hematopoietic stem cell transplantation (HSCT) is an effective curative therapy for a long list of hematological malignancies. Historically HSCT was the only mode of therapy that could provide a cure for a long list of hematological malignancies including acute myeloid leukemia (AML), acute lymphatic leukemia (ALL), and myelodysplastic syndrome which are the main indications for HSCT in Europe; but also for chemosensitive non-Hodgkin lymphomas (NHL), Hodgkin lymphoma, and multiple myeloma (MM), the main indications for autologous transplantation. However, transplantation could be offered to only a rather small fraction of the patients in need due to the high risk

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of toxicity and mortality of the procedure especially in patients with comorbidities for age and performance status. But also due to the organ toxicity of the pre-HSCT, conditioning, and transplant-related complications, mainly graft versus host disease (GVHD). On the other hand, allogeneic transplantation mediating the graft versus tumor effect that correlates with GVHD provided the first demonstration of cellular immunotherapy and the ability to tailor the immune system against malignancies. The immune system can recognize and eliminate malignant cells and as such is a powerful tool in fighting cancer.

This was the basis for the development of donor lymphocyte infusions,nonmyeloablative conditioning, and finally the chimeric antigen receptor -T (CAR-T) adoptive immunotherapy that revolutionized anti-cancer therapeutics.

CAR-T cell therapy for hematologic malignancies turns out to be a cutting-edge therapeutic advancement that is leading the immunotherapy frontier and cancer therapy. CD19-specific CARs for lymphatic malignancies including NHL, MM, and ALL revolutionized the field and changed completely treatment paradigms in lymphatic hematological malignancies. Currently, there are 6 commercial CAR-T cell products that are FDA-approved (4 for NHL and ALL and 2 for MM). In general, the toxicities of CAR-T cell therapy are lower than those of HSCT, there are no age limits and CAR-T is effective in patients with chemoresistant, high-risk diseases that failed HSCT. In NHL they are offered already in the second line of therapy and as a result, the number of autologous transplantations is being sharply reduced in NHL and MM. However, there are major issues with the availability and affordability of CAR-T cell therapy, and many patients that are in need cannot receive it, especially in low or medium-income countries. Point-of-care academic CAR T cells may overcome these limitations. We, at Sheba Tel- Hashomer, initiated already in 2016 a point-of-care academic CAR-T cell program in which hundreds of patients with relapsed/refractory ALL, NHL patients (first as the third line, and then patients failing the first line of therapy or relapsed within 12 months), and from 2021 patients with MM are being treated with CD19 and anti-B cell maturation antigen (BCMA) based CAR-T cells, respectively. We also treated a small cohort of patients with AML harboring the 8:21 translocation that expressed CD19 with CAR-T cells. The benefits of point-of-care CAR-T cells are a shorter time, 10-11 days, from a vein (leukapheresis) to the vein (administration) and therefore, almost no need for bridging therapy but mainly lower cost significantly increasing CAR-T cells affordability and accessibility. We will try to discuss these issues in our session.

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Sp03

The revolution in frontline treatment of Multiple Myeloma

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The frontline treatment of multiple myeloma has recently been revolutioned, thanks to the approval of a new backbone, daratumumab, anti-CD38 monoclonal antibody, in both transplant-eligibile and -not eligibile patients.

In transplant-eligible setting, daratumumab has been added, according to CASSIOPEIA trial, to the previous standard-of-care bortezomib-thalidomide-dexamethasone (Dara-VTD), followed by autologous-stem cell transplantation (ASCT), two cycles of consolidation, and oral lenalidomide maintenance until progression.

In transplant-ineligible setting, daratumumab is added, according to MAIA trial, to lenalidomide-dexamethasone (DRD) until progression, or, according to ALCYONE Trial, to bortezomib-melphalan-prednisone (Dara-VMP) x 9 cycles.

Results are incredible in both settings in terms of efficacy and tolerability, with the achievement of very good quality of life for patients, also thanks to the schedules and the subcutaneous administration of daratumumab.

Achieving the deepest response correlates with the best long term result, and that's why, in this scenario, the endpoint becomes not only the achievement of complete response/stringent complete response, but also MRD negativity. That's why the importance of testing accurately the results of the treatment, particularly evaluating MRD during the patient journey, also in real world, is becoming more and more important, not only in order to optimize the use of the drugs, also in maintenance setting, but also to balance correctly efficacy and toxicity.

Ongoing trials are also aiming to evaluate the role of new generation agents, in new quadriplets with potential deepest results but also risk of greater toxicities for which supportive care needs to be improved and standardized.

In next future, ongoing clinical trials aim to evaluate the role of new agents in induction regimens, and also anti-BCMA CAR-T in replacing ASCT, together with the role of bispecific antibodies in maintenance setting, and the idea of MRD-driven approach potentiating or reducing the treatment according to the response.

CAR-T have shown excellent results in heavily pretreated patients, with the limits of tolerability and feasibility, also for costs: the increasing opportunities for academic products could help to improve and optimize the use and also to better evaluate these agents in a less selected population.

Another interesting perspective is to anticipate the treatment, before the onset of symptoms, concentrating efforts on correctly diagnosing and treating high-risk Smoldering myeloma, strongly waiting for results coming from phase 3 trials aiming to compare IMIDs with the combination anti-CD38 antbody, IMIDs and dexamethasone, avoiding ASCT, and permitting to the patients to obtain deep response with a really good tolerability.

In conclusion, in frontline setting, considering the wonderful opportunities that we have in real world, and that are coming in next future, our endpoint, should be to achieve the deepest responses, aiming to MRD negativity, particularly in young and fit patients, balancing with tolerability and quality of life.

This should become the new endpoint of upcoming clinical trials, considering that its achievement could correlates with the best long-term response and could really help us and our patients to the cure of multiple myeloma.

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Sp04

CML 2023 - State Of The Art And Cutting Edge İssues

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Chronic myeloid leukemia (CML) and its treatment is the prototype of translational research and success of targeted therapy. It was the first disease with a definitive molecular marker where specific targeted small molecular inhibitors, tyrosine kinase inhibitors (TKIs), changed dramatically the course and prognosis from a fatal disease into one with nearly normal survival. TKIs in clinical use are imatinib, nilotinib, dasatinib, bosutinib and ponatinib. Asciminib is a newly developed allosteric BCR-ABL1 inhibitor. Clinicians can personalize treatment based on the toxicity profile of TKIs, taking into account patients' age, comorbidities and lifestyle. Despite the revolution in the treatment and prognosis of CML in the last 3 decades we are still facing some challenges: Vascular adverse events have emerged as a serious side effect of some TKIs and treatment, especially of elderly patients, and this should be taken into consideration. While treatment of chronic phase CML is considered a great success, coping with accelerated and especially blastic phase CML is still a big challenge. The role of allogeneic stem cell transplantation (alloSCT) and donor lymphocyte infusion (DLI) in 2024 is minor but still relevant for some patients. Future treatments combining TKIs with checkpoint inhibitors as well as interferon or asciminib are under investigation. The issue of deep molecular response (DMR) and its implications for treatment discontinuation and treatment free remission (TFR) – who, when and why, has clinical as well as emotional and financial considerations. Matters of quality of life (QOL) and patient reported outcome measures (PROMs) are now in the forefront once the disease changed its course from a fatal to a chronic and even curable one. And finally, can we look into a crystal ball to predict at the outset who will respond to therapy, who will achieve DMR and who will benefit from prolonged TFR and cure.

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Sp05

Management Of Early Relapsed Follicular Lymphoma Debate Favoring Non-Transplant Options

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Follicular lymphoma (FL) is the most common non-Hodgkin lymphoma in the United States and Europe[1]. The disease is potentially incurable and, treatment options comprise a wide spectrum from local radiotherapy to chemoimmunotherapy, based on the risk factors. The outcome of follicular lymphoma patient requiring treatment significantly improved with the introduction of rituximab[2,3]. Rituximab or obinituzumab in combination with cyclophosphamide, adriamycin, vincristine, prednisolone (G/R-CHOP) or with bendamustine (BR/OR) are preferred in the frontline setting[4]. RELEVANCE study showed that lenalidomide-rituximab (R2) has similar efficacy to R-chemotherapy approach in the first-line treatment[5].The response rate to first-line chemoimmunotherapy is around 65% and, about 20% of the cases responding to chemoimmunotherapy experience progression of disease within 24 months (POD24) and have poorer overall survival[6,7]. Current prognostic scores are not efficient to predict POD24 cases.

AUGMENT study showed improved efficacy with R2 compared to R in the second line treatment of indolent lymphomas. Eighty-three percent of the cases had FL and 31% of the cohort experienced POD24. The overall response rate (ORR) was 78%, with an improved 2-year progression-free survival rate of 58% compared to 36% with R alone[8]. MAGNIFY study evaluating R2 maintenance following R2 induction reported an ORR of 65% and a median PFS of 27.4 months for POD24 group[9].

Tazemetostat is an oral EZH2 inhibitor. EZH2 is mutated in 20-30% of FL patients. It offered an ORR of 69%, with a median PFS of 13.8 months in early relapsed FL cases with EZH2 mutation. Although the ORR was lower compared to late relapsing cases, the PFS was longer in EZH2 mutant group compared to 5.8 months in wild-type cases[10]. Copanlisib,a pan-class I phosphatidylinositol 3-kinase inhibitor was evaluated in a phase II study in both indolet and aggressive lymphoma patients. The ORR was 58.7% in indolent lymphoma patients[11]. Chronos-3 trial revealed that when copanlisib was combined with rituximab, median PFS was improved to 21.5 months compared to 13.8 months with R monotherapy[12]. Idealisib, duvelisib and umralisib removed their indications for relapsed and refractory FL due to a trend toward lower overall survival (OS) in patients exposed to these agents[13].

CAR-T cell therapy changed the treatment paradigm in B-cell lymphomas. In the ZUMA-5 trial, Axicabtagene ciloleucel reported an ORR of 92% in both POD24 and without POD24 cohort.The 18-months estimated duration of response, PFS and OS rates were 60%, 55% and 85% in POD24 cases, whereas they were 78%, 84% and 94% in patients without POD24[14]. Treatment with Tisagenlecleucel showed lower complete response rates in POD24 patients compared to those without POD24, reported to be 59% vs 87.9%[15].

Treatment with bispecific antibodies, suc as epcoritamab, mosutetuzumab and glofitamab, constitute an alternative to CAR-T. The ORR ranged between 80% and 90% with bispecific antibody monotherapy in early-relapsing FL cases[16-18].

Nonchemotherapeutic approaches have promising outcomes and are currently preferred in second line setting for POD24 patients. The role of stem cell transplantation in controversial in FL. However, there is not any solid data comparing transplantation with nonchemotherapeutic options.

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Sp06

Treatment Of Classical Hodgkin Lymphoma: The State Of The Art

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WHERE WE ARE?

Patients with advanced-stage classical Hodgkin lymphoma (cHL) have a good prognosis. In most countries, the first-line treatment has been, for at least a couple of decades, the ABVD protocol. Depending on several factors such as age, presence of *bulky* disease, or extranodal involvement, around 75-80% of patients are cured with this regimen[1]. However, there are now new treatment recommendations for advanced-stage cHL. After 6 years of follow-up, the ECHELON-1 study showed overall survival (OS) benefit for brentuximab vedotin with AVD versus the standard ABVD[2]. This has never happened in previous direct comparative trials. Although the BV+AVD was already approved for first-line treatment of advanced-stage cHL patients, based on the gain of progression-free survival (PFS) published a couple of years ago, a benefit in OS makes a much stronger case. Peripheral neuropathy was a special concern, with about 2 out of 3 patients treated with BV+AVD experiencing some form of symptom. Mainly it was grades I 1 and 2, and the symptoms did resolve or improved in almost 90% of cases[2]. But the BV-AVD reign has already been challenged. The SWOG1826 study is a randomized, multicenter, phase 3 trial, that compares the combination of nivolumab with AVD (nivo-AVD) versus BV-AVD[3]. This is a large trial, with almost 1000 patients, that included patients between 12 and 83 years. The 1-year PFS rate was 94% versus 86% (HR 0.48, 99%CI 0.27-0.87; p=0.0005), in favor of Nivo-AVD. OS was similar (99% vs 98%), with a short median follow-up of 12.1 months. Interesting that both arms of this study were for a limited number of 6 cycles, something different that is normally done with checkpoint inhibitors (usually until the progression of the disease, unacceptable toxicity, or up to 2 years). So, a longer follow-up will be paramount to see if this advantage for nivo-AVD will hold in time. The toxicity profile was largely as expected and no new safety signals in both arms. On the other hand, the HD21 study looked at the association between BV and a similar backbone of the escalated BEACOPP (eBEACOPP), known as BrECADD[4]. This new regimen was compared in a multicenter, randomized, phase 3 non-inferiority trial, with the standard eBEACOPP. Using a PET-adapted strategy, where interim PET negative patients completed 4 total cycles versus 6 total cycles in PET positive, BrECADD was non-inferior to eBEACOPP. The 3y-PFS rate was 94.9% versus 92.3%, with a median observation time of 40 months. These impressive results compare favorably with BV-AVD in the ECHELON-1 study (6y PFS of 82.3%) and with Nivo-AVD in the SWOG study (1y PFS of 94%), but with all the restrictions of comparing different trials.

WHAT TO EXPECT FOR THE FUTURE?

Clearly, in one of the lymphomas with the best overall prognosis, the treatment landscape evolved. There are now at least 3 new options for the treatment of advanced-stage cHL in the first line, with better results than ABVD, the standard for a long time. As we continue to improve efficacy, toxicity remains an important issue. Longer follow-ups will be needed to see if we can have great results without impact in our patient's quality of life.

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Sp07

MDS 2023: State of The Art

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The myelodysplastic syndromes (MDS) are clonal bone marrow (BM) stem cell disease(s), characterized by abnormal hematopoiesis, with anemia (95%) and/or other cytopenias. The pathogenesis is based on genetics and inflammation of aging (inflammaging). The median age of onset is 74yr, with increasing incidence with age. Patients are classified as having a lower (LR-MDS) or higher risk disease (HR-MDS), and leukemic transformation occurs in 20%-60%.

We will cover new aspects like quality of life (QoL), novel genetic information, will briefly touch the emerging field of inflammaging, describe new tools for (early) diagnosis, the new classifications, and finally will address MDS treatment. We will skip aspects such as epidemiology, clinical picture and cytogenetics.

Over the last decade QoL has become important in MDS, to study and improve – we will show some data. Genetics is an integral part of evaluation, with at least one mutation in 90% of MDS patients, but as more information is obtained it has become clear that the field is quite complex. The pathogenesis is carefully investigated and inflammation of aging (inflammaging) appears to play an important role.

Diagnosis of MDS has been recognized as a challenge. The introduction of new tools, such as genetic and digital medicine improve the process, make it more accurate, less invasive, and hopefully may identify individuals at risk.

Several new MDS classifications (and guidelines) have been proposed over the last couple of years. We will focus on the new IPSS-Molecular model, and will summarize the 5th WHO and ICC classifications.

RBC transfusions and erythropoietin (EPO) remain the 1st line treatment for anemia in lower-risk MDS. EPO is safe and might delay the need for RBC transfusions. A recent EUMDS study suggests a prolonged survival with EPO. Lenalidomide remains effective for MDS with del(5q) (50% response), but also somewhat effective (27%) in non-del(5q) patients. Luspatercept appears as an effective second-line (maybe 1st ?) agent. Several experimental agents are investigated, including oral azacytidine, imetelstat, a pyruvate-kinase activator and roxadustat. For thrombocytopenia two agents, romiplostim and eltrombopag, were shown to be effective. However, due to safety concerns their development has been stopped.

Treatment of higher-risk MDS is still based on hypomethylating agents (HMA) as the standard 1st line treatment, but attempts are ongoing to overcome the barrier of 50% response rate and less than 2 years response duration. Younger patients may respond to antileukemic treatment with or without transplant. Ways to improve the HMA effect include treating the HMA-related complications; modified HMA formulation; combinations of HMA with other agents (venetoclax appears to be the frontrunner), novel agents and targeted molecules.

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Sp08

Blastic Plasmacytoid Dendritic Cell Neoplasm BPDCN

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy with an aggressive clinical course and poor prognosis. BPDCN is most often characterized by its presentation with cutaneous lesions which are often asymptomatic, can be solitary or multiple lesions, can be distributed widely, and may range from bruise-like lesions to plaques or nodules. Bone marrow involvement, central nervous system (CNS) infiltration, lymphadenopathy, splenomegaly, and/or cytopenias are also seen to varying degrees.

The nomenclature has changed many times over the years, making descriptions of the epidemiology more challenging. It was first described in 1995 as acute agranular CD41 natural killer (NK) cell leukemia. In the most recent WHO 2022 classification, BPDCN is classified under dendritic cell and histiocytic neoplasms along with plasmacytoid dendritic cell proliferation associated with myeloid BPDCN is more common in older men, with a sex ratio of 3:1 to 5:1 and a median age of diagnosis between 60 and 70 years. A bimodal age distribution was recently described, with higher incidence in patients aged ,20 and .60 years.

BPDCN cells characteristically express CD123, CD4, CD56, CD303, TCF4, and TCL-1, whereas certain specific lineage markers such as CD14, cCD3, CD19, and MPO are not expressed.

Genetic mutations implicated in the pathogenesis of BPDCN include inactivating tumor suppressors (ie, TP53, RB1, CDKN1B, and CDKN2A), activating oncogenes (ie, NRAS, KRAS, FLT3, RUNX2, and HES6), activated NF-κB pathway, mutated RNA spliceosomes (ie, ZRSR2 and others), immune response gene dysregulation (IFNGR, TGFB, CLEC4C, and IFNA cluster), and epigenetic dysregulation (ie, IDH1, IDH2, TET1, TET2, and ASXL1).

Historically, BPDCN treatments have been based on multiagent chemotherapy regimens for lymphoma, acute lymphoblastic leukemia, and AML. In addition, acute leukemia regimens achieve high complete response (CR) rates ranging from 40–90% and allogeneic hematopoietic cell transplantation (allo-HCT) can result in durable remission in some patients. However, their rarity and heterogeneity make it difficult to determine the most effective therapeutic strategies.

Owing to recent advances in molecular biology and genetics, targeted treatment strategies have been developed. In 2018, the FDA approved tagraxofusp, a firstin-class CD123-targeting therapy for treatment- naïve or relapsed/refractory BPDCN.However, unfit, relapsed, or refractory patients continue to require effective therapeutic strategies.

Besides CD123 Targeted therapy; many other modalities are considered e.g. Venetoclax-based therapy, Transplantation and many new potential therapeutic targets under investigation.

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Sp09

Sustained Remission and Decreased Severity of CAR T-Cell Related Adverse Events: A Pivotal Study Report of CNCT19 (inaticabtagene autoleucel) Treatment in Adult Patients with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-Cell ALL) in China

Lv Lulu

Juventas Cell Therapy Ltd

A B S T R A C T

CNCT19 (inaticabtagene autoleucel) is an autologous CD19-specific chimeric antigen receptor (CAR) T-cell product. The patent protected CAR structure of CNCT19 contains a unique CD19 scFv, HI19a, which is different from commonly used FMC63. Together with using 4-1BB co-stimulatory domain in the CAR structure, CNCT19 is expected to reduce the severity of treatment-associated cytokine release syndrome (CRS) and neurologic toxicities (NT) while maintaining a stronger and longer durable anti-tumor effect.

CNCT19 has been granted Breakthrough Therapy Designation by China National Medical Products Administration and Orphan Drug Designation by the U.S. FDA for the treatment of ALL.

The trial of CNCT19 in adult Chinese patients with R/R B-cell ALL (NCT04684147) is a single-arm, open-label pivotal study conducted at 10 centers in China. The primary endpoint was the overall complete response rate (OCR) of complete response (CR) and CR with incomplete hematological recovery (CRi) within 3 months and at the end of Month 3 after CNCT19 infusion by central assessment.

All 39 patients diagnosed with B-cell ALL were refractory and relapsed to multiple lines of prior therapy. Among the 39 patients 32 (82.1%) had reached MRD-negative OCR within 3 months after CNCT19 infusion, The median duration of response and OS have not been reached. 25 patients (64.1%) remained on CR (51.3%) or CRi (12.8%). at the end of Month 3 after CNCT19 infusion These patients had sustained long-term remission regardless of whether subsequent allo-HSCT treatment was done or not. The most common CNCT19-related adverse events (AEs) were CRS and NT and there were

4 cases of Grade ≥ 3 CRS (n=4, 10.3%) and 3 cases of Grade ≥ 3 NT (n=3, 7.7%). Following CNCT19 infusion, all the patients recovered. No death cases were reported due to CRS or NT.

CNCT19 CAR-T cell therapy achieved a high rate of MRD-negative complete remission in adult patients with R/R B-cell ALL. Thus, with its distinct CAR structure containing a unique CD19 scFv (HI19a), CNCT19 provides effective treatment with potential long-term clinical benefits for adult patients with R/R B-cell ALL.

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Sp10

Personalized Dendritic Cell Vaccines

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Due to their ability to cross-present antigens associated with tumor cells to naive T cells, DCS play an important role in generating specific T-cell-mediated antitumor effector responses in controlling tumor growth and tumor cell dissemination. Clinical trials in this area have demonstrated the possibility of immunotherapy based on dendritic cells. In the current study, we give a brief overview of the biology of DC, describe the sources of obtaining tumor-associated antigen, and also consider the current status of the field of application of DC as anti-cancer vaccines.

Methodology: Peripheral blood mononuclears were used in the work, as well as lung tumor cells, from which tumor lysate was obtained. Tumor lysate was obtained by freezing and thawing a cell suspension by placing an ampoule with cells in liquid nitrogen or warm water, respectively. Dendritic cells were obtained by culturing human peripheral blood monocytes. The key cytokines used in the cultivation of DC from monocytes are GM-CSF and interleukin-4 (IL-4). DC was loaded with antigens after replacing the culture medium with the addition of tumor lysate to the cells and incubation for 2 hours. The main way to assess the quality of the vaccine created on the basis of DC was the method of flow cytofluorimetry. The main characteristics by which DC is evaluated are the immunophenotype and the percentage of living cells.

Conclusion: The proven method of obtaining dendritic cells loaded with tumor lysate makes it possible to apply this approach more widely in oncological practice. The use of an antitumor vaccine based on autologous dendritic cells for the prevention of relapses may become a new way of adjuvant treatment.

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Sp11

CPi -Clalit Proactive and Preventative Intervention

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Clalit is the largest HMO in Israel that insures more than 4.7 million people and the second HMO worldwide after Kisser in USA. CPi - Clalit Proactive and Preventative Intervention, is the flag project innovation of clalit community division, in collaboration with clalit research institute and clalit digital division. This innovation combines big data, medical databases, artificial intelligence and a complex computer algorithm, which guides the doctor during the visit, to provide evidence-based personalized knowledge.

No more, surrogate outcomes but rather pure major events outcome. The vision - Patients will receive a proactive and preventive care suitable to their current condition based on the most updated clinical guidelines in an attempt to reduce the gaps in good clinical practice and combined them together to a pure handy knowledge for the primary care physician. The former name of the project Was POEMS -Patient oriented evidence that matters meaning we treat our patients in order to improve their morbidity and to reduce their mortality.

For example, Diabetes is a major issue at the primary care clinic. When I started to practice medicine there were 3-treatment option: Sulphonyls urea Metformin and Insulin. Unfortunately, nowadays there are more than 60 drugs on the shelf, each one of them with pros and cons, and as the one responsible for the evidence based care, it is hard and almost impossible to remember the names, the inclusion criteria and the adverse effect of each drug concerning the patient history.

We used the current guidelines from the American Diabetes Association and converted those guidelines to the Israeli basket aiming to give the right medication to the right patient considering the patient morbidity as; Atherosclerotic disease, Heart Failure, and Chronic Kidney Disease. Expert committees create an ideal "clinical pathway" for each clinical condition and so, patients “travel” through these pathways every single day and gather their personalized recommendations. CPI can advise to add another diabetic medication for the patient, while taking into account his cardiac, kidney and liver functions. Detailed Explanation is available for each recommendation from Dynamed (wwwdynamed.com)

This is already happening nowadays, more than 1500 physicians, half of the primary care physician at Clalit use this platform.

In 7 years the WHO is aiming to declare the world as free from hepatitis C. In march 2023 we added, hepatitis C as a major issue at CPi. We developed strict algorithm by Artificial Intelligence according to patient's risk factors. The patients are sent to Antibody Blood test (AB for Hepatitis C). People

with positive AB will automatically pass PCR test, those that are positive will be presented to the physician at the CPI screen, guiding him to prescribe one out of the two anti-viral treatment for hepatitis C while checking beyond the screen the cross reaction between the patient chronic medications and the new viral medication against Hepatitis C .

BY the end of 2023 we are going to launch our last version of hypertension treatment according to the new version of the JNC as the same manner as diabetes. Couple of weeks later we will launch the CPI model for primary CVD treatment according to the evidence based guidelines supported by remote monitoring at the patient own and comfort environment using blood pressure gauge and glucose sensors that can broadcast the output directly to the patient record and CPi.

CPi is a breakthrough platform for Clinicians. Our routine quote for the busy physician is that 3 clicks for an answer are 2 clicks too much.

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