Conclusions: Pleural infiltrating T-cells represent an attractive source of T cells for immunotherapy. They are numerous, readily expandable without protracted passage and can be induced to secrete immunostimulatory and effector cytokines and specifically kill autologous tumor.

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SP 18

Are there really cancer stem cells and how do they operate?

Robert Gale

Some but not all data suggest within a cancer not all cancer cells are the same, namely, there are diverse cell types. The *stem cell* theory of cancer proposes amongst all cancer cells a very few act as *stem cells*. These cells reproduce themselves and sustain the cancer much like normal stem cells renew and replenish organs and tissues like the haematopoietic system. There are important therapy implications if cancers are really driven by a few *stem cells*. For instance, many anti-cancer therapies are evaluated based on their ability to make a cancer smaller. This can happen without killing cancer *stem cells*. If so, the cancer is likely to recur, perhaps in a more dangerous form such as metastases. In fact, most people with cancer die from metastases, not the primary cancer. The analogy is selecting a more virulent microbe by indiscriminate use of antibiotics.

One component of the cancer *stem cell* theory concerns how cancers arise. Typically, for a cell to become cancerous it must accumulate substantial numbers of mutations. A leukaemia such as chronic myeloid leukaemia (CML) is an exception caused by 1 mutation (*BCRABL1*). Conventional cancer theory is that any cell has the potential to become a cancer. However, other data suggest only some cells, those with *stem cell* potential, can develop into a cancer. This may explain why some normal people can have cancer-related mutations without having cancer, for example normals with *BCRABL1* or normals with t(14;18) without CML or without a lymphoma. The hypothesis is the cell(s) in which these mutations occur are not *stem cells* and therefore lack the potential to cause cancer. However, we must also consider the possibility some mutations can re-programme a cell without *stem cell* potentially to become a *stem cell*. An example of this are induced pluripotent stem cells iPSC) which are adult (non-stem) cells reverted to an *embryonic stem cell* state by introducing 4 genes. Another notion is only cells with *stem cell* like features survive sufficiently long to accumulate the typically large number of mutations required for cancer development. The theory, therefore, is cancer *stem cells* arise from normal *stem cells* or *precursor cells* produced by normal *stem cells*.

Another important implication of the cancer *stem cell* theory is cancer *stem cells* are closely related to normal *stem cells* and share many properties. Cancer cells produced by cancer *stem cells* should follow many of the rules observed by normal daughter cells. In this regard cancer cells can be considered a caricature of normal cells with similar but distorted features. If so, it may be possible to use knowledge about normal *stem cells* to identify and attack cancer *stem cells*.

Lastly, it may not be necessary to eradicate all cancer stem cells to cure a cancer. For example, in CML, therapy with tyrosine kinase-inhibitors (TKIs) markedly reduces numbers of mature leukaemia cells but not any and certainly not all CML *stem cells*. Regardless, in a substantial proportion of people with CML responding favorably to TKI-therapy it is possible to stop therapy without leukaemia returning. In sum, increasing knowledge of cancer stem cells should improve our understanding of and ability to treat diverse cancers.

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SP 19

Challenges in treating solid tumors in developing countries

Adnan Abdul Jabbar

There is an increasing number of cancers worldwide due to epidemiological transition. Longer life spans resulting in aging population is among some of the reasons for growing burden in cancer worldwide. The number of new cancer cases is expected to increase by nearly 75% by 2030 (107,000 additional cases per annum), with 60% of cases in the elderly (aged ≥65). The extent of cancer related morbidity and mortality is directly linked to the effectiveness of efforts to prevent, control and treat cancer, particularly in the developing world. In 2012, almost 57% of all cancer cases and 65% of cancer deaths occurred in low-and middle-income countries. If the current trend continues, the burden of cancer will increase to 22 million new cases annually by 2030, with 81% of new cases and almost 88% of mortality occurring in less developed countries. Cancer care in a country like Pakistan is challenging because of lack of strategic information and national planning for cancer control. Cancer registry provides important information that helps in directing and planning cancer prevention and care. Lack of national cancer registry limits estimation of true burden, identification of areas that require special need and thereby proper treatment strategy. Health systems required to deliver comprehensive life-saving treatments are limited in the country. Out of pocket payments and private health care usage remains high. A number of patients are not covered by insurance and individuals face catastrophic expenditure in seeking treatment. As a result, there is disparity in access to quality care. High incidence of later stage disease is very common due to social stigma associated with cancer treatment, myths, lack of awareness and preference for alternative treatment options. Drugs that have lately revolutionized cancer management are either not available in the country and if present, are extremely expensive for a common person to afford. Palliative care and access to supportive care medicines is almost nonexistent. Pain management is restricted to analgesics without narcotics. With cancer rates steadily rising in low- and middle-income countries, the disease will inevitably

frustrate global development efforts unless urgent action is taken.

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SP 20

Lymphoblastyc lymphoma/leukemia: a single center experience

Alina Antipova, Olga Baranova

Introduction: Lymphoblastic lymphoma (LBL) is a rare neoplasm of lymphoblasts or precursor T- and B-cell with predominantly involves lymph nodes, mediastinum or extranodal tissues with minimal persistence in bone marrow. LBL amount 2% of all non-Hodgkin lymphomas. T-phenotype is the most common one and reaches above 80% of LBL. LBL and acute lymphoblastic leukemia (ALL) have the same biological entity according WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues 2017. Distinguishing criterion between two diseases is the number of bone marrow blasts 25%. ALL-regimen provide better overall (OS) and disease-free survival (DFS) in contrast with CHOP-like schemes.

Patients and methods. A retrospective review of LBL patients from **N.N. Blokhin National Medical Research Center of Oncology** (Russia, Moscow) during period between 2009 and 2020 was done. Patients were treated according ALL-2009 protocol (Russian ALL-Study Group, ClinicalTrials.gov NCT01193933). Kaplan–Meier curves and log-rank test were used to evaluate the OS and DFS. This study includes 20pts with primary ($n=15$) and relapse LBL ($n=5$). T-cell LBL pts were 18, and 2 were of B-cell lineage. Most patients were males 85% (17 of 20). Stage II and IV both at 45%, stage III 10%. All T-LBL patients showed a mediastinal tumor, B-LBL pts had involved peripheral lymph nodes and soft tissues. The rate of LBL among all primary lymphoid precursor neoplasms (LBL and ALL) was 17.6%. Median follow up was 28 months (0.5–170.5 mo).

Results: All 5 relapse patients were pre-treated out of our center: after CHOP-like treatment with relapse in initial zones and all died from disease ($n=3$), after HyperCVAD, later followed alloHSCT ($n=1$, alive) and 1 pts after ALL-BFM-2002 with mediastinum and CNS relapse. CR rate of primary LBL ($n=15$) was 93%, 1 pts was refractory and later died. Radiotherapy has been carried out in 40% (6 of 15) patients with residual tumor mass after chemotherapy consolidation. 1 patient was been undergoing autoSCT. The 10-year OS of patients with LBL, T-ALL and B-ALL was 73.8%, 48.7% and 54.5% respectively ($p=0.3$). The 10-year DFS in the same groups was 75%, 56.3% and 64.5% respectively ($p=0.2$). Although the results are not statistically significant, we see a trend towards better survival outcomes in patients with LBL. AlloSCT was performed in 2 patients LBL in CR2, one of them alive, the other died of complications.

Conclusion: The results of treatment of LBL pts in **N.N. Blokhin National Medical Research Center of Oncology** are comparable to most of the similar reported studies. The survival results of LBL patients with ALL-regimen therapy seem to be better compared with patients ALL. CHOP-like chemotherapy is a very poor prognostic factor for LBL patients. The role of autoSCT has not been developed. In our center we have satisfied outcomes of LBL with minimal rate of high dose consolidation with autoSCT. Radiotherapy at postconsolidation phase in patients with residual tumor mass reduces the risk of relapse.

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SP 21

Relapsed and refractory classical Hodgkin lymphoma immunotherapy

Kirill Lepik

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Background: Introduction of PD-1 inhibitor nivolumab (Nivo) into a clinical practice revolutionized the treatment of relapsed and refractory classical Hodgkin lymphoma (r/r cHL). Yet there is a set of unresolved clinical questions including the assessment of response, the prognostic factors influencing the survival of patients during immunotherapy, and optimal treatment strategy in patients resistant to nivolumab, as well as the possibility of discontinuation of therapy in case of persistent complete remission. This report presents the results of analysis of nivolumab treatment outcomes in Pavlov University.

Methods: This retrospective study included r/r cHL patients treated with standard-dose nivolumab (3 mg/kg q2w). Therapy was continued until the disease progression, signs of intolerance or could be stopped at the discretion of treating physicians in selected patients with prolonged complete remission. In patients with r/r disease after nivolumab monotherapy, 48 received nivo and bendamustine (Benda) in a 28-day cycle. Benda (90 mg/m^2) was infused on day 1,2 and Nivo – on day 1 of the cycle. The response was assessed by PET-CT scan every 3 months according to LYRIC criteria.

Results: The analysis included 116 patients treated with nivolumab monotherapy (56 m/60 f) with a median age of 32 years (range 14–63). With a median follow-up of 41 (6–54) months after treatment initiation, 108 (93%) patients were alive, the median OS was not reached. Median PFS was 19 mo (13.7–24.4) with a 3-year PFS of 27%. The best overall response was CR in 33%, PR in 34%, SD in 5%, PD in 9%, an indeterminate response (IR) in 20% of pts. Patients with early CR at 3mo after treatment initiation had significantly better prognosis (median PFS 35 mo vs. 17 mo, $p=0.008$). Other clinical factors that predicted prognosis were B-symptoms (median PFS 15 mo vs. 26 mo, $p=0.017$), extranodal disease at the moment of the treatment initiation (median PFS 14 mo vs. NR, $p=0.000$), >4 prior lines of therapy (median PFS 18mo vs. 27 mo, $p=0.05$). In a group of patients ($n=23$) who discontinued nivolumab in complete response (CR), the possibility of durable remission achievement was demonstrated (2-year PFS was 55.1%). The nivolumab retreatment has demonstrated the efficacy with high overall response rate (ORR) and CR (67 and 33.3% respectively). In the group of patients receiving nivo-benda combination after nivolumab monotherapy failure, the