Abstract Highlights

The following highlights focus on several insightful and innovative abstracts at the European Hematology Association (EHA) 2022 hybrid congress, covering topics such as gene mutations in acute myeloid leukaemia and the use of B cell maturation antigen-targeted chimeric antigen receptor T cells extracted from cord blood in the treatment of patients with multiple myeloma.

Secondary Mutations in Patients with *de Novo* Acute Myeloid Leukaemia

RESEARCHERS have uncovered a number of gene mutations in patients diagnosed with *de novo* acute myeloid leukaemia (AML). Amongst these, a set of mutations such as *SRSF2, ZRSR2, ASXL1, SFB31, STAG2, U2AF1, EZH2*, and *BCOR* have been categorised as secondary AML-type mutations, with a distinct distribution in secondary AML when compared with primary AML.

The aim of the study, carried out jointly by the departments of Haematology, Oncology, and Pathology at the National Taiwan University Hospital, Taipei, Taiwan, and the National Taiwan University Cancer Center, Taipei, Taiwan, was to explore both the clinical significance and prognostic implications of secondary AML-type mutations in patients without non-M3 AML.

The study enrolled 921 patients with *de novo* non-M3 AML, 368 of whom were aged 60 or over. Patients were excluded if they had an antecedent history of haematologic diseases or therapy-related AML. Secondary AML-type mutations were found using targeted next-generation sequencing of 54 myeloid malignancies, which are related to gene mutations.

Researchers found that 243 patients (26.4%) in the ST group had secondary AML-type mutations. This patient group was generally older and, at diagnosis, had lower white blood cell counts, peripheral blast counts, and lactate dehydrogenase levels. Of the patients receiving standard chemotherapy (n=686), those in the ST group had a shorter overall survival rate (median 2.1 years versus not reached; p<0.01) and disease-free survival rate (median 0.4 years versus 0.9 years; p<0.01) with a median follow-up of 4.7 years.

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Analyses carried out within subgroups discovered that secondary AML-type mutations had impacts on the prognosis of patients, both with regard to overall survival (median years: 5.8 versus 1.5 versus 1.3 for patients with 0, 1, and >2 mutations, respectively), and disease-free survival (median years: 0.9 versus 0.6 versus 0.0 for those with 0, 1, and >2 mutations, respectively). These findings occurred across both younger and older patient groups. Among patients with secondary AML-type mutations, allogeneic haematopoietic stem cell transplantation improved outcomes (median overall survival: 3.0 versus 0.8 years; p<0.01). ●

Acute Myeloid Leukaemia Relapse Following Allogeneic Stem Cell Transplant

A SINGLE institution retrospective study has been carried out by researchers at the Institut Paoli Calmettes, Marseille, France, into relapses of patients with acute myeloid leukaemia (AML) who have received allogeneic stem cell transplant. They focused on a sample of 118 patients from their institution, who relapsed following allogeneic stem cell transplant between January 2009 and December 2019.

Relapse of disease has, in recent years, become the main cause of treatment failure in patients diagnosed with AML, replacing transplant-related mortality. The risk of relapse after allogeneic stem cell transplant is around 30%, but this depends heavily upon both clinical and genomic elements. Due to the variability in disease characteristics, there exists no standard of care for patients, and prognosis is consequently poor; the survival rate after 2 years is reported to be only 20%. In some cases, patients with AML can undergo a first-line treatment of intensive chemotherapy, and then a second-line cellular therapy treatment such as allogeneic stem cell transplant or donor lymphocyte infusion.

In this study, median age was 53. Twenty-two percent of patients had *FLT3* mutations and 53% an adverse genetic risk; 79% had received a transplant; and 21% still had active disease. Forty-five per cent of patients were given an allograft from a related donor; 22% from an unrelated donor; 18% from a haplomismatch related donor; 10% received an allograft from cord blood cells; and 5% from a mismatched unrelated donor.

Researchers found that the median time from allogeneic stem cell transplant to relapse was 4.7 months. Seventeen patients in the group underwent a second round of allogeneic stem cell transplant; 13 of these after intensive salvage, one after non-intensive salvage, and six had active disease. Early transplant mortality following allogeneic stem cell transplant was 25%. The median follow-up of patients alive was 70.2 months (46.3–83.5).

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The researchers' data supported the findings of existing studies and confirmed the poor prognosis and outcome of post-transplant relapse in patients with AML. They found that whilst intensive salvage therapy does show a reasonable response rate, subsequent cellular therapy appears to be necessary for long-term disease-free survival. ●

Cord Blood BCMA-CAR-T Cells in Treatment of Multiple Myeloma

RESEARCHERS in China have studied the safety and efficacy of B cell maturation antigen-targeted chimeric antigen receptor (BCMA-CAR)-T cells extracted from cord blood in the treatment of patients with both refractory and relapsed multiple myeloma, the second most common haematologic malignancy worldwide.

The prognosis of patients with multiple myeloma varies. Low-risk patients can survive for more than 10 years with standard care; however, high-risk patients have a prognosis of around 1 year. Whilst CAR-T cell therapy has had promising results in clinical trials, it is not always possible to generate clinically significant amounts of these cells from heavily pre-treated patients and, therefore, it is not a treatment that can be used effectively for every patient.

This study acknowledges that whilst allogeneic CAR-T cell therapy could potentially be used instead, there is a risk of graft-versus-host disease. Cord blood has a good supply of T cells, which have a low immunogenicity, and a relatively low risk for the patient of developing graft-versus-host disease.

Investigators from from the Shaanxi Provincial People's Hospital, Xi'An, China; Shanghai Jiao Tong University, China; and Northwest University, Xi'An, China, have collaborated on a study that incorporates cases recorded between January and December 2021 in Shaanxi Provincial People's Hospital. Cluster of differentiation 3+ T cells were chosen, activated, and modified using lentivirus in order to produce anti-BCMA-CAR-T cells. After expanding for 5–10 days *in vitro*, these cells were then administered intravenously to patients with refractory and relapsed multiple myeloma who had received lymphodepleting chemotherapy treatments 2–3 days previously.

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Eleven patients were selected for the study (seven male; four female), with a median age of 58 years. Two patients had received previous CAR-T cell therapies and relapsed before enrollment. Seven patients had been given autologous haematopoietic stem cell transplantation. All patients received the average dose of 7.11×106 /kg. CAR-T cells were found to have increased in every patient, with no increase in levels of IL-6, 1L-8, and interferon receptors in peripheral blood 2 weeks after infusion. One patient relapsed after 3 months of follow-up and another patient died from severe pulmonary infection.

The research team concluded that there is a promising safety profile surrounding CAR-T cells derived from cord blood, and the treatment could work effectively for patients who are ineligible for autologous CAR-T cell therapy, as well as preparing them for future treatment regimens. ●

Outcomes and Responses of COVID-19 Vaccine in Patients With Severe Aplastic Anaemia

ACCORDING to a study on the COVID-19 vaccine in patients with severe aplastic anaemia (SAA), SAA could result in a temporary decline in blood counts. SAA is a potentially fatal bone marrow failure disorder that presents with pancytopaenia and a hypocellular marrow due to immune-mediated destruction of haematopoietic stem cells. Due to neutropenia and treatment with immunosuppressive therapy (IST) patients are at a higher risk of infection.

The aim of the study was to examine the impact of the severe acute respiratory syndrome coronavirus 2 vaccine on SAA disease status and to establish the humoral and cellular response to vaccine. The researchers analysed the blood samples from 50 patients diagnosed with SAA, involving 29 females and 21 males, with mean age of 42 years (9–78). SAA was managed with IST including horse antithymocyte globulin, cyclosporine, and eltrombopag at the National Institute of Health (NIH). The included participants had received the COVID-19 vaccine between January and November 2021. The SAA disease status during the vaccination time was reported as either response, partial response (PR), and non-response.

The results showed that 94% of the patients did not have changes in the status of the disease after receiving the vaccine. There were 15 patients (30%) receiving cyclosporine as treatment. Progressive or significant decline in blood count, also defined as relapse after receiving vaccine, was reported in 3 cases (6%). The three relapsed patients were deemed weak PR at time of vaccination (platelet count: <50 k/μL) and were 6 months, 3 years, and 4 years from initial IST, respectively. Out of the three patients, two had only received one of the Pfizer (New York City, New York, USA) vaccines and not the second due to a decline in the blood count. The third patient had received the Moderna (Cambridge, Massachusetts, USA) complete set of vaccines and demonstrated a relapse at 4 weeks and a decline in blood counts 6 months before vaccination.

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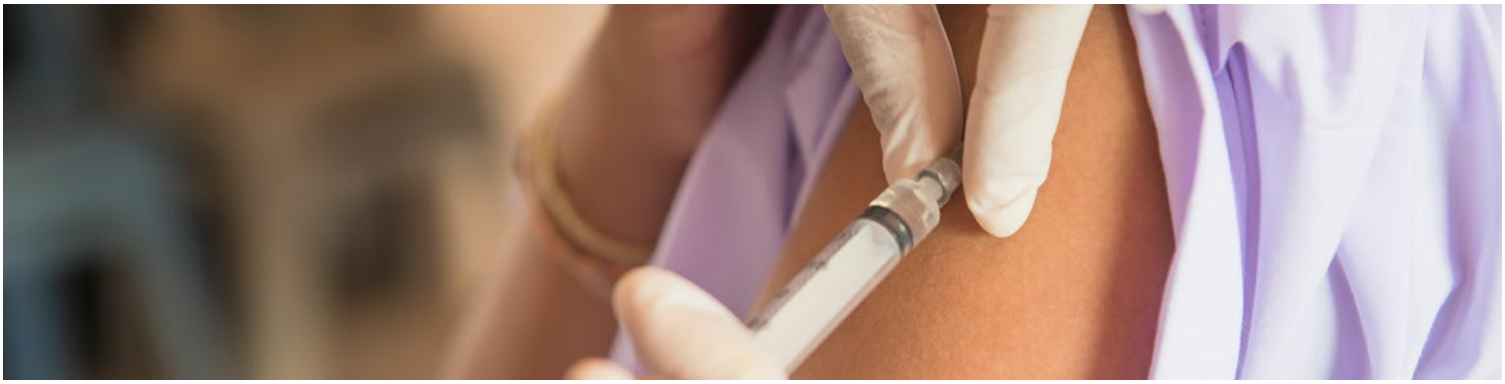
The study concluded that true relapse is rare, but the COVID-19 vaccine could result in temporary decline in blood counts. However, the relapse is more probable in patients who had a blood count decline prior to vaccination. Further research including a risk versus benefit evaluation is needed to confirm COVID-19 vaccination in patients with SAA weak PR to initial therapy. ●



Association Between Vitamin D Levels and Cardiac Iron with Function in Patients with Thalassaemia Major

Researchers from the Fondazione Toscana G. Monasterio, Pisa, Italy, investigated the association between vitamin D (vitD) levels and cardiac iron with function in patients with thalassaemia major (TM). Decreased vitD levels are widely understood to stimulate the expression of transmembrane L-type voltage-dependent calcium channels, which absorb both calcium and iron. However, there is currently little evidence defining the correlation between vitD levels and cardiac iron.

Investigators examined myocardial iron overload in 278 patients with TM pulled from the Extension-Myocardial Iron Overload in Thalassemia Network. They collected further data on left ventricular function parameters using cine images and measured serum 25-hydroxyvitamin D/calcifediol using chemiluminescent immunoassay. Furthermore, vitD supplements were provided to 61.4% of patients.

Results of the investigation demonstrated that vitD levels were deficient in 107 patients (38.5%), insufficient in 96 patients (34.5%), and adequate in 75 patients (27.0%). No significant difference was detected between male and female patients; however, patients with deficient vitD were found to be significantly younger than patients with adequate vitD (36.96±7.64 years compared with 39.63±9.39 years; p=0.042). Pivotally, patients with deficient vitD levels had significantly higher risk for myocardial iron overload than patients with adequate vitD levels (odds ratio: 20.62; 95% confidence interval: 2.67–153.72; p=0.004).

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Examining other patient parameters, researchers found significantly higher left ventricular (LV) end-diastolic volume index and LV mass index in patients with deficient compared with patients with normal vitD levels. Furthermore, though no statistical difference was detected a tendency towards LV ejection fraction was found in patients with vitD deficiency that the other groups.

From their results, the research group concluded that in TM vitamin D deficiency was associated with increased risk of cardiac iron overload, and that regular assessment of vitD levels may contribute to the prevention of both bone disorders and cardiac iron accumulation with its associated dysfunction. ●