Research for Tomorrow

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At this time of the year, hemato-oncologists worldwide eagerly await the latest results from clinical trials and real-world studies being presented at the American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA) annual meetings. Immunotherapy in particular, including cell-based therapies, is rapidly advancing. New chimeric antigen receptor (CAR) T constructs are being developed at breathtaking speed and the indications for approved products are constantly expanded. CAR T-cells have become an integral part of lymphoma treatment and several CD19-directed CAR T-cell therapies have entered the market. Recently, axicabtagene ciloleucel (axi-cel, YESCARTA®) was approved by the Food and Drug Administration (FDA)[1] for the treatment of patients with large B-cell lymphoma (LBCL) who are refractory or relapsed (R/R) after first-line chemo-immunotherapy, based on the results of the phase III ZUMA-7 study.[2] Additionally, tisagenlecleucel (tisa-cel, KYMRIAH®) received approval from the European Commission[3] (EC) and was granted accelerated FDA[4] approval for the treatment of adult patients with R/R follicular lymphoma (FL) after ≥2 lines of systemic therapy. Brexucabtagene autoleucel (brexu-cel, TECARTUS®) is a second-generation CD19-targeted CAR T-cell therapy that was approved for patients with R/R mantle cell lymphoma (MCL) in Switzerland[5] and across Europe,[6] based on the results of the ZUMA-2 study.[7] Brexu-cel is also approved in the US for the treatment of adult patients with R/R acute B-cell precursor acute lymphoblastic leukemia (ALL).[8] Moreover, lisocabtagene maraleucel (liso-cel, BREYANZI®) received approval from the European Medicines Agency (EMA)[9] for the treatment of adult patients with R/R LBCL after ≥2 of systemic therapy.

This unprecedented clinical success of CAR T-cell therapies in B-cell malignancies was more recently extended to the field of multiple myeloma. In 2022, idecabtagene vicleucel (ide-cel, ABECMA®), a B-cell maturation antigen (BCMA)-directed CAR T-cell therapy, entered clinics in Switzerland for the treatment of heavily-pretreated adult patients with R/R multiple myeloma.[10] Based on the findings of the phase Ib/II CARTITUDE-1 trial,[11] ciltacabtagene autoleucel (cilta-cel, CARVYKTI®), another BCMA-directed CAR T product, was approved in the US this year for the treatment of adult patients with heavily pretreated R/R multiple myeloma.[12]

Treating physicians collect, study and present "real-world data", which teach us how to identify patients who will benefit most. Studies on *in vivo* and *ex vivo* immunomodulation are ongoing and are important to improve existing CAR T products. This is exciting for patients with R/R lymphoma and myeloma, as these treatments promise to replace high-dose chemotherapy and stem cell transplantation in these indications and potentially may cure some patients with previously incurable conditions.

However, even in wealthy countries such as Switzerland, the question of the impact of such expensive therapies on the health budget and how this can be maintained is increasingly being raised. Further, how it is morally justifiable to spend huge financial sums on a small selected patient population in rich countries, in times of war, imminent famine for large parts of the world's population and the climate crisis. The immediate, direct health consequences of war are mostly obvious and recognizable. Indirectly, the war in Ukraine may cause an even greater number of fatalities. On one hand, there will be increased mortality due to the lack of effective treatments for patients with various diseases, which is challenging to measure. Even more so, the implications of the impending famine in Africa and other parts of the world due to a lack of grain supplies will be severe. According to the United Nations Security Council meeting in May 2022 "around the world, 44 million people in 38 countries are at emergency levels of hunger, noting the Russian Federation's invasion of its neighbor has effectively ended Ukraine's food exports, with a price increase of up to 30% for food staples, threatening people in countries across Africa and the Middle East".[13] In contrast, the World Health Organization (WHO) estimates an annual cancer death rate of approximately 10 million per year.[14] The failure to ensure sufficient food for a growing world population

is impacted by politics and is dramatically aggravated by the serious effects of climate change: the increasing frequency of heat waves is resulting not only in drought, affecting agricultural crop production, but also has direct consequences on the health of the human body.[15,16]

Science is a robust and effective tool that has the potential to find real solutions to these global problems. It is not an easy, quickly available enterprise but requires long-term support and investment from the state and society. Only this way it can back up scientists and give them the space to develop new strategies. A recent example of the power of science is the development of the SARS-CoV-2 vaccination in just a few months, based on research subsidies of all parties involved. Similarly, research in the field of alternative energy and food sources must be supported and advanced, for only science and sound research will be able to solve the major global challenges in the coming decades.

We as cancer researchers have significant public visibility. We can use our visibility and strengths to advocate for sound science and research. In times of alternative facts and fake claims on social media, we need to be very clear about how scientifically sound results are generated and integrity is ensured. The true value of science needs to be shown more clearly and this may be our contribution in these challenging times.

Please do not hesitate to provide your feedback and enjoy reading this edition.

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