HAEMATOLOGICAL CANCER

KTE-X19 active in MCL

The survival outcomes of patients with relapsed and/or refractory mantle-cell lymphoma (MCL) after receiving BTK inhibitors are poor; therefore, new treatment options are needed for these patients. Chimeric antigen receptor (CAR) T cell therapies targeting CD19 have demonstrated efficacy in several subtypes of B cell lymphomas, although limited results in patients with MCL have been reported. Now data from the ZUMA-2 trial reveal promising activity of the anti-CD19 CAR T cell product KTE-X19 against MCL.

In ZUMA-2, KTE-X19 was successfully manufactured for 71 of 74 patients with relapsed and/or refractory MCL. A high content of leukaemic blasts in peripheral blood has been proposed as the cause of failed manufacturing of CAR T cells because it results in proportionally low numbers of non-exhausted T cells in the starting cell population. During the manufacturing of KTE-X19, circulating $CD19^+$ malignant cells were removed in order to address this issue by reducing the potential activation and exhaustion of anti-CD19 CAR T cells in the ex vivo portion of the process.

KTE-X19 was administered to 68 patients. Among 60 patients with at least 7 months of follow-up monitoring, the objective response rate (ORR) was 93%, with a complete response (CR) rate of 67%. ORRs were consistent across patient subgroups, including those with high-risk disease. At a median of 12.3 months, 57% of the 60 patients and 78% of those with a CR had an ongoing response. Of note, all these patients received a single infusion of KTE-X19.

Exploratory analyses of minimal residual disease revealed that 24 of 29 patients (83%) and 15 of 19 patients (79%) had no detectable residual disease at 4 weeks and 6 months, respectively. The 12-month progression-free survival and overall survival estimates were 61% and 83%, respectively.

Grade ≥3 adverse events (AEs) occurred in 99% of 68 patients, the most common of which were cytopenias (94%) and infections (32%). Grade 1–2 and ≥3 cytokine-release syndrome (CRS) occurred in 76% and 15% of patients, respectively. Two infectious AEs were fatal. All CRS events resolved with treatment within a median of 11 days. Grade 1–2 and ≥3 neurological AEs occurred in 32% and 31% of patients. These events resolved with treatment in 37 of 43 patients (86%) at a median of 12 days. No deaths resulted from CRS or neurological AEs.

In conclusion, the results of ZUMA-2 indicate that patients with relapsed and/or refractory MCL can derive clinical benefit from CAR T cells, although at the expense of a high risk of toxicities. The majority of AEs reported in this trial were manageable. Moreover, the toxicity profile of KTE-X19 was deemed similar to that of the CAR T cell products used to treat patients with other B cell lymphomas. Longer follow-up results will help to determine the durability of these responses; in addition, the results of other trials of CAR T cell products in patients with MCL are eagerly awaited.

Diana Romero

ORIGINAL ARTICLE Wang, M. et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. *N. Engl. J. Med.* **383**, 1331–1342 (2020)

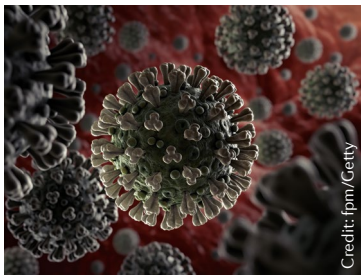
EPIDEMIOLOGY

COVID-19 and cancer: what we know so far

Infection with SARS-CoV-2, resulting in coronavirus disease (COVID-19), can lead to acute respiratory distress syndrome (ARDS) requiring admission to an intensive care unit (ICU), and sometimes death, in a subset of patients. So far, we know that individuals ≥60 years of age and/or those with a supressed immune system are particularly vulnerable to COVID-19, although how these risks apply to patients with cancer remains unclear. Several reports are beginning to emerge.

First, patients with cancer seem to be more likely to be diagnosed with COVID-19. Among 1,524 patients admitted to the Department of Radiation and Medical Oncology of Zhongnan Hospital of Wuhan University, 12 (0.79%) had COVID-19, versus 0.37% of the general population of Wuhan during the same period of time (OR 2.31, 95% CI 1.89–3.02). In the same study, patients with non-small-cell lung cancer (NSCLC) seemed to have a higher incidence of COVID-19, especially those >60 years of age (4.3% versus 1.8% in those aged ≤60 years with NSCLC).

Second, patients with cancer seem to have more severe COVID-19 symptoms than those without. In a retrospective analysis, the outcomes of 28 patients with cancer and COVID-19 admitted to one of three hospitals in Wuhan for quarantine and treatment of COVID-19 have been described. Of these patients, 10 (35.7%) had stage IV disease at the time of admission; lung cancer was the most common cancer type, in 7 patients (25%). As of February 26th, 15 patients (53.6%) had developed severe clinical events (those requiring mechanical ventilation or ICU admission), 10 patients (35.7%) had life-threatening complications and 8 (28.6%) had died. Most deaths (5) were caused by ARDS; other causes of death included pulmonary embolism, septic shock, and acute myocardial infarction. By comparison, among the general population with confirmed COVID-19,


Credit: fpm/Getty

4.7% had severe clinical events and 2.3% of patients died. Receiving the most recent cancer treatment within 14 days (HR 4.1, 95% CI 1.09–15.32; $P = 0.037$) and patchy consolidation on chest CT (HR 5.44, 95% CI 1.50–19.75; $P = 0.010$) were both associated with severe clinical events among those with cancer.

These findings are supported by a nationwide analysis of data from 2,007 cases of COVID-19 from 575 hospitals across China. In this cohort, the 18 patients with COVID-19 and cancer had a higher incidence of severe events (39% vs 8%; $P = 0.0003$), and receiving chemotherapy or surgery in the past month was found to further increase this risk following adjustment for other variables (OR 5.34, 95% CI 1.80–16.18; $P = 0.0026$).

Despite many limitations, including low numbers of patients, the retrospective nature of the evidence and the limited follow-up durations, these data provide early insights into how the management of patients with cancer might be affected by the COVID-19 pandemic. Notably, patients with cancer seem to be both more likely to be diagnosed with COVID-19 and have more severe symptoms. In this scenario, oncologists need to weigh up the balance of risks versus benefits carefully when planning normally routine cancer treatments and follow-up appointments.

Peter Sidaway

ORIGINAL ARTICLES Yu, J. et al. *JAMA Oncol* https://doi.org/10.1001/jamaoncol.2020.0980 (2020) | Zheng, L. et al. *Ann. Oncol.* https://doi.org/10.1016/j.annonc.2020.03.296 (2020) | Liang, W. et al. *Lancet Oncol.* **21**, 335–337 (2020)