**Website address:**
https://www.gesundheitsindustrie-bw.de/en/article/press-release/cancer-patients-receiving-immunotherapy-no-evidence-increased-risk-severe-immune-complication-after-covid-19-vaccination

# Cancer patients receiving immunotherapy: no evidence of increased risk for severe immune complication after COVID-19 vaccination

**Does COVID-19 vaccination increase the risk of cancer patients undergoing therapy with immune checkpoint inhibitors to suffer a dangerous immune complication known as a "cytokine release syndrome"? A team of Heidelberg physicians and scientists has now shown in a clinical study: Increased serum levels of the characteristic cytokines occur frequently in cancer patients, but clinically relevant cases of the dreaded syndrome were not observed. The result supports the current recommendation to vaccinate cancer patients against COVID-19, even under therapy with immune checkpoint inhibitors.**

*Joint press release from the National Center for Tumor Diseases (NCT) Heidelberg, the German Cancer Research Center (DKFZ), Heidelberg University Hospital (UKHD), and the German Cancer Consortium (DKTK).*

Does COVID-19 vaccination increase the risk of cancer patients undergoing therapy with immune checkpoint inhibitors to suffer a dangerous immune complication known as a "cytokine release syndrome"? A team of Heidelberg physicians and scientists has now shown in a clinical study: Increased serum levels of the characteristic cytokines occur frequently in cancer patients, but clinically relevant cases of the dreaded syndrome were not observed. The result supports the current recommendation to vaccinate cancer patients against COVID-19, even under therapy with immune checkpoint inhibitors.

According to the German Robert Koch Institute, cancer patients are considered a risk group for severe courses of COVID-19 disease. For this reason, many patients consider it particularly important to protect themselves against the viral disease with a vaccination against COVID-19.

But is the Corona vaccination associated with special risks for people with cancer? Today, more and more cancer patients are being treated with a so-called "immune checkpoint inhibitor", often shortened to "immunotherapy". Immune checkpoint inhibitors block signals that cancer uses to slow down the immune system's T cells. The agents release the brakes on the immune system, reactivating the immune response against tumor cells.

"There was concern that immune checkpoint inhibitors could trigger strong, uncontrolled immune responses in vaccinated individuals," says Guy Ungerechts, senior physician in the Department of Medical Oncology at Heidelberg University Hospital and National Center for Tumor Diseases (NCT) in Heidelberg, Germany, and head of the Virotherapy Clinical Cooperation Unit at the German Cancer Research Center (DKFZ) and Heidelberg University Hospital (UKHD). Excessively activated T cells can trigger a dreaded cytokine release syndrome (CRS). This complication, which manifests itself with high fever, falling blood pressure, oxygen deficiency and, in extreme cases, multi-organ failure, can occur when activated immune cells release large quantities of messenger substances called cytokines.

"In order to provide the best possible advice to our patients, we wanted to find out whether CRS actually occurs frequently after corona vaccination when treated with immune checkpoint inhibitors. In addition, we wanted to clarify whether the determination of CRS-associated cytokines in the blood could be an early indication of the development of clinically manifest CRS," explains Thomas Walle, the lead author of the current study, who is a physician at the NCT Heidelberg and conducts research in the department headed by Guy Ungerechts at the DKFZ and in the German Cancer Consortium (DKTK).

In a prospective study, the oncologists at the NCT Heidelberg examined 64 vaccinated and 26 unvaccinated cancer patients undergoing therapy with immune checkpoint inhibitors. The study participants suffered from 23 different types of cancer. From the first vaccine dose to four weeks after the second vaccination, patients were monitored for adverse events. None of the patients experienced clinically relevant CRS. Nevertheless, certain cytokines characteristically associated with CRS were elevated to approximately 1.5 times baseline levels in 40 percent of participants after vaccination.

"Under therapy with immune checkpoint inhibitors, COVID vaccination appears to frequently trigger the release of CRS-associated cytokines but rarely causes symptoms," says Sunanjay Bajaj. "Cytokine measurements alone are therefore unlikely to be useful in assessing the risk of CRS." The first author of the current study conducts research as a medical student in the collaborative unit led by Guy Ungerechts, as well as in the DKTK.

Among the vaccinated patients, physicians also observed improved overall survival, which could not be explained solely by

higher COVID-19-related mortality among the unvaccinated. "Of course, our result needs to be validated by a study with a larger number of cases," Guy Ungerechts said. "But for now, our data support the current recommendation to cancer patients on immune checkpoint inhibitor therapy to take advantage of vaccination against COVID-19 to protect against severe courses of viral infection."

**Publication:**
Thomas Walle, Sunanjay Bajaj, Joscha A. Kraske, Thomas Rösner, Christiane S. Cussigh, Katharina A. Kälber, Lisa Jasmin Müller, Sophia Boyoung Strobel, Jana Burghaus, Stefan M. Kallenberger, Christoph K. Stein-Thöringer, Maximilian Jenzer, Antonia Schubert, Steffen Kahle, Anja Williams, Birgit Hoyler, Lin Zielske, Renate Skatula, Stefanie Sawall, Mathias F. Leber, Russell Z. Kunes, Johannes Krisam, Carlo Fremd, Andreas Schneeweiss, Jürgen Krauss, Leonidas Apostolidis, Anne Katrin Berger, Georg M. Haag, Stefanie Zschäbitz, Niels Halama, Christoph Springfeld, Romy Kirsten, Jessica C. Hassel, Dirk Jäger, NCT ANTICIPATE Investigators and Guy Ungerechts. Cytokine release syndrome-like serum responses after COVID-19 vaccination are frequent and clinically inapparent under cancer immunotherapy. Nature Cancer 2022, DOI: https://doi.org/10.1038/s43018-022-00398-7

**Press release**

23-Jun-2022
Source: German Cancer Research Center

**Further information**

- German Cancer Research Center (DKFZ), Heidelberg
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- University Hospital Heidelberg
- German Cancer Consortium