Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COVID-19 vaccines in patients with cancer

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Navigating uncertainties generated by structural barriers to scientific evidence is often challenging. For instance, the systematic exclusion of patients with cancer from the pivotal clinical trials of COVID-19 vaccines is arguably almost inexcusable.[1] Patients with cancer have been included in the priority category for vulnerability to COVID-19 since the early phases of the pandemic.[2] There is, therefore, an urgent need to better understand the efficacy and safety of COVID-19 vaccines in immunosuppressed individuals, as recurrent exclusion of these and other vulnerable groups from ongoing studies of COVID-19 vaccines will result in imprecise predictive health models, which will in turn have consequences on successive waves of the pandemic.[3]

In *The Lancet Oncology*, Leticia Monin and colleagues[4] aimed to address this issue by providing some clarity on the safety and immunogenicity of COVID-19 vaccines in patients with cancer. The authors report the first analysis of a prospective, longitudinal, observational study (SOAP-02) that enrolled patients with cancer who received the mRNA-based SARS-CoV-2 BNT162b2 vaccine (Pfizer–BioNTech). Not all participants received the boosting second dose at 3 weeks; after initiation of the SOAP-02 study, a decision was made by the UK Government on Dec 30, 2020, to deviate from the recommended protocol and prolong the interval between the two doses from 3 weeks to 12 weeks.

The population health impact of this policy decision by the UK Government remains unclear.[5] Modelling exercises show that the decision to postpone the second dose could be acceptable in non-vulnerable populations; this decision was justified on the basis of the high seroconversion rates observed after the first dose, and the persistence of immune protection at the time of the second dose.[6] Legitimate criticisms about this strategy were addressed, especially about the impact of delayed vaccine boosting on older, vulnerable populations—a priority group with substantially lower rates of immediate seroconversion and more severe outcomes from COVID-19 than younger, healthy groups.[7] All of these considerations had to be contextualised against the emergence of the SARS-CoV-2 variants of concern, for which vaccine-derived immune protection has not been reported as comprehensively.[7,8]

In the SOAP-02 study, the authors analysed the safety and efficacy of the BNT162b2 vaccine in 151 patients with cancer (95 with solid cancer and 56 with haematological cancer), as well as in a non-age-matched group of 54 healthy controls, and aimed to understand the impact of the first dose in patients with cancer after 3 weeks.[4] The cancer population was heterogeneous, with a median age of 73·0 years, 64% of patients had at least one adjunctive non-communicable comorbidity, and almost half were exposed to different anticancer treatments both before and after the first dose of the vaccine. The healthy control cohort comprised mostly health-care workers, was younger (median age 40·5 years) and healthier (no comorbidities), with twice as many Black, Asian, and minority ethnic individuals as the cancer cohort.

At 3 weeks, 94% (95% CI 81–98) of healthy controls had mounted an immune response (IgG positive titres against the SARS-CoV-2 spike protein) with a single dose.[4] Conversely, only 38% (95% CI 26–51) of patients with solid cancers and 18% (10–32) with haematological malignancies had seroconverted. Poorer responders were identified as those with respiratory and skin cancers, and those receiving the vaccine within 15 days of chemotherapy. Viral neutralisation assays reported inferior efficacy in patients with cancer, with T-cell responses remaining unaltered or declining after the first dose. Notably, the authors showed that a single dose was ineffective at neutralising the variant of concern B.1.1.7 strain, which is up to 90% more transmissible than the Wuhan wild-type strain and responsible for up to 98% of SARS-CoV-2 infections reported in the UK at present, thus governing the current pandemic trajectory.[8]

Following the second dose at day 21, 95% (95% CI 75–99) of patients with solid cancer seroconverted, with nearly half being de-novo positive to anti-S IgG antibodies.[4] The boost increased both specific IgG titres and in-vitro capacity to neutralise the wild-type and B.1.1.7 strains. For patients who were not boosted, no spontaneous change in the immunisation trajectory was observed.

These findings stress the importance of pursuing evidence-based health policy, especially in vulnerable populations.[4] Errors in estimations, speculative assumptions, and extrapolations from data about other vaccines can have a substantial impact on current and successive pandemic waves, detrimentally affecting population health: at present, the data suggest that

vulnerable individuals should be prioritised for an early (21-day) second dose of the BNT162b2 vaccine, to avoid exacerbating the pandemic threat.[3,6,7] This is a particularly sensitive issue as new variants of concern are being increasingly reported, with uncertainties about the efficacy of the currently available vaccines against these emerging strains.[9] Maximising vaccination efficacy and coverage is one way to tackle the emergence of variants of concern.[7,9]

It is therefore important to prioritise those populations that can derive the greatest benefit from vaccination against SARS-CoV-2, and thus have a positive impact on the trajectory of the ongoing pandemic.[7] High-priority groups should include patients with cancer and their close contacts (eg, non-professional carers).[10] The implementation of alternative vaccine schedules is not inconsequential and can often affect the efficacy of vaccines.[6] Similarly, adapting the schedules to account for the risk of severe outcomes from COVID-19, and the capacity of individuals to mount and maintain an immune response, is very important.[7,10] Customising vaccination schedules could be one way to formulate more efficient health policies that are data driven.

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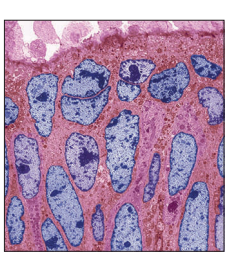
Trastuzumab deruxtecan: heralding biomarker-directed therapy in metastatic colorectal cancer

Biomarker-directed therapy is increasingly being used to treat metastatic colorectal cancer, including using *RAS* mutational status to select patients for EGFR antibodies use, mismatch repair deficiency to select patients for treatment with PD-1 and CTLA-4 antibodies, and, more recently, *BRAF* mutational status to select for treatment with encorafenib plus cetuximab.

DESTINY-CRC01,[1] reported in *The Lancet Oncology* by Salvatore Siena and colleagues, evaluated trastuzumab deruxtecan in patients with HER2-expressing metastatic colorectal cancer, reporting an objective response in 24 (45·3%; 95% CI 31·6–59·6) of 53 patients in the HER2-positive cohort (primary endpoint). Median progression free survival and overall survival were not reached, at a relatively short follow-up of 4·1 months (IQR 2·8–5·7) and 5·4 months (4·1–8·3), respectively, in those who were HER2-positive. However, in this cohort, objective response rate in patients with HER2-positive immunohistochemistry (IHC3+) was notably higher (57·5%; 95% CI 40·9–73·0) than that in patients with HER2 IHC2+ and in-situ hybridisation (ISH) positive tumours (7·7%; 0·2–36·0), although the patient number in the latter group was small (n=13). Responses appeared to be durable and were seen irrespective of previous HER2-targeted therapy, suggesting a degree of non-overlapping resistance. However, no responses with trastuzumab deruxtecan were observed in HER2 moderately-expressing, without gene amplification, metastatic colorectal cancer or HER2 low-expressing metastatic colorectal cancer, suggesting that in these subgroups, response and disease control was not adequate. These results echo, and might even surpass, other recent studies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