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.

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LETTERS TO THE EDITOR

Commentary: SARS-CoV-2 vaccines and cancer patients

Since the first reports of coronavirus disease 2019 (COVID-19), severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) infection has affected more than 79 million people worldwide, prompting the World Health Organization to declare a public health emergency in late January 2020 and a pandemic in March 2020.[1] Higher mortality of COVID-19 seems to be related to cancer, but data are inconsistent.[2] Of note, most biological agents and immunotherapy do not seem to increase mortality in this setting.[2]

Although an optimal treatment of COVID-19 remains uncertain, pre-pandemic care will return as soon as an effective vaccine strategy becomes available. To date, 44 vaccine candidates are being evaluated for prevention of COVID-19 in phase I clinical trials, followed by 21 and 18 vaccine candidates investigated in phase II and III trials, respectively.[3] These include nucleic acid-based vaccines, viral-vector vaccines, inactivated or recombinant protein vaccines.[3] In early-phase trials, numerous vaccines have induced binding antibodies, neutralizing activity, and T cell responses in healthy adults.[3] A few candidates seem to be immunogenic in healthy older individuals, as well.[3]

For people with cancer, immunization recommendations have been developed by the Infectious Diseases Society of America (IDSA). In general, patients receiving chemotherapy or other immunosuppressive agents should not receive live vaccines and should generally not receive inactivated vaccines. Although SARS-CoV-2-specific IgG antibody response does not seem to be different between healthy subjects and cancer patients,[4] it is unknown whether an effective immunization will be achieved in this subset of people. In this regard, data about how many individuals with a history of cancer have been involved in all phase III vaccine trials are lacking. Yet, eligibility of cancer patients can be deduced from inclusion and exclusion criteria of the trials, since some manufacturers made their full study protocols publicly available.[5] Interestingly, most protocols excluded cancer patients on the basis of conditions that can be summarized in three categories (Table 1): (i) any prior history of cancer; (ii) recent immunosuppressive therapies (chemotherapy, radiotherapy, immunomodulating agents, systemic immunosuppressants); (iii) immunodeficiency and lack of stable disease, at the discretion of the investigator.

Moreover, sample size estimates were based on the basis of low control event rates (CERs) for some trials, suggesting that ~99% of placebo recipients are not expected to develop symptomatic COVID-19.[5] Understandably, such study designs, with symptomatic COVID-19 of any severity as a primary endpoint, low CER estimates, and many interim analyses are justified by the need for fast results rather than focusing on severe disease, amidst a global health care emergency.[5] That said, people at higher risk, like cancer patients, who should be sensibly prioritized to receive an approved vaccine, may be underrepresented in ongoing phase III clinical trials (Table 1).

In conclusion, manufacturers and investigators should be encouraged to provide real-time data about the characteristics of recruited participants, preferably including clearly identifiable subgroups, like cancer patients, with sample sizes large enough to determine safety and efficacy in these categories as well.

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Table 1. COVID-19 vaccine candidates approved or in phase III trials as of 22 December 2020

Vaccine	Developer	Immune features	Clinical Trial Identifier	Exclusion criteria for cancer patients	Demographic data (if available)
mRNA-1273 (lipid nanoparticle-mRNA)	Moderna/NIAID	Expressing S protein; two repeated i.m. doses	NCT04470427 Phase III ongoing. Emergency authorization by FDA.	People who have received systemic immunosuppressants or immune-modifying drugs for >14 days in total within 6 months before screening.	No cancer patients enumerated at interim data analysis.
Comirnaty BNT162b2 (lipid nanoparticle-mRNA)	BioNTech, Pfizer, Fosun Pharma	RBD of S protein; two repeated i.m. doses	NCT04368728 Phase III ongoing. Full approval in Bahrain, Canada, and Saudi Arabia; emergency authorization by FDA and EMA.	People receiving immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, e.g. for cancer.	No cancer patients enumerated at interim data analysis.
Ad5-nCoV/Convidecia (non-replicating adenovirus type 5 vector)	CanSino Biologics	Expressing S protein; single i.m. dose	NCT04526990 NCT04540419 Phase III ongoing. Limited emergency approval in China.	People with current diagnosis of or treatment of cancer (except basal cell carcinoma of the skin and cervical carcinoma *in situ*).	No demographic data published or posted on ClinicalTrials.gov.
Gam-Covid-Vac (Sputnik V) adenovirus-based (rAd26-S+rAd5-S)	Gamaleya Research Institute	Single dose and heterologous Ad26 prime; Ad5 boost i.m. doses	NCT04530396 (RESIST) NCT04564716 Phase 3 ongoing. Emergency approval in Russia and Belarus.	History of any malignant tumors.	n.a.
Ad26.COV2.S/JNJ-78436735 (adenovirus type 26 vector)	Beth Israel Deaconess Medical Center and Johnson & Johnson (Janssen)	Expressing S protein; two repeated i.m. doses	NCT04505722 (ENSEMBLE) NCT04614948 (ENSEMBLE 2). Phase 3 ongoing.	Malignancy within 1 year before screening, except squamous and basal cell carcinomas of the skin and carcinoma *in situ* of the cervix, or other malignancies with minimal risk of recurrence. Patients receiving CT, immune-modulating drugs or RT within 6 months before administration of vaccine and/or during the study.	No demographic data published or posted on ClinicalTrials.gov.
ChAdOx1 nCov-19 (AZD-1222) (non-replicating viral vector)	University of Oxford/ AstraZeneca	Expressing S protein; two repeated i.m. doses	NCT04516746 NCT04540393 (COV002 and COV003) ISRCTN89951424 CTRI/2020/08/027170 Phase III ongoing.	History of primary malignancy except for malignancy with low potential risk for recurrence after curative treatment or metastasis (for example, indolent prostate cancer) in the opinion of the site investigator.	No demographic data published or posted on ClinicalTrials.gov.
NVX-CoV2373 (protein subunit)	Novavax	Recombinant S protein; two repeated i.m. doses	(UK) 2020-004123-16/2019nCoV-301 (USA) NCT04611802/2019nCoV-301 Phase III ongoing.	(UK) Current diagnosis of or treatment of cancer (except basal cell carcinoma of the skin and cervical carcinoma *in situ*, at the discretion of the investigator). (USA) Active malignancy on therapy within 1 year before first study vaccination (with the exception of malignancy cured via excision, at the discretion of the investigator).	No demographic data published or posted on ClinicalTrials.gov.
CoVLP (plant-derived VLP adjuvanted with GSK or Dynavax adjuvants)	Medicago/GSK	Two repeated i.m. doses	NCT04636697 Phase III ongoing.	Any confirmed or suspected immunosuppressive condition, including cancer. Investigator discretion is permitted. People receiving cytotoxic, antineoplastic, or immunosuppressants within 36 months before vaccination.	No demographic data published or posted on ClinicalTrials.gov.
COVID-19 vaccine (protein subunit)	Chinese Academy of Medical Sciences/ Anhui Zhifei Longcom	Two or three repeated i.m. doses	NCT04466085 (phase II) Phase III ongoing.	History of any malignant tumors.	n.a.

Continued

Table 1. Continued

Vaccine	Developer	Immune features	Clinical Trial Identifier	Exclusion criteria for cancer patients	Demographic data (if available)
BBIBP-CorV (Vero cell, inactivated)	Wuhan Institute of Biological Products/ Sinopharm	Multiple viral antigens; two repeated i.m. doses	NCT04560881 NCT04612972 Phase III ongoing. Limited emergency approval in China and UAE.	History of any malignant tumors.	n.a.
BBIBP-CorV (Vero cell, Inactivated)	Beijing Institute of Biological Products/ Sinopharm	Multiple viral antigens; two repeated i.m. doses	NCT04560881 NCT04510207 Phase III ongoing. Full approval in UAE and Bahrain. Limited emergency approval in China.	History of any malignant tumors.	n.a.
CoronaVac (inactivated)	Sinovac Biotech	Multiple viral antigens; two repeated i.m. doses	NCT04456595 (PROFISCOV) 669/UN6.KEP/EC/2020 NCT04582344. NCT04617483 Phase III ongoing. Limited emergency approval in China.	Use of CT or RT within 6 months before enrollment or planned use within the 2 years following enrollment. History of malignancy or antineoplastic CT, RT, immunosuppressants in the past 6 months.	No demographic data published or posted on ClinicalTrials.gov.
Covaxin (inactivated)	Indian Council of Medical Research/ Bharat Biotech	Multiple viral antigens; two repeated i.m. doses	CTRI/2020/11/028976 Phase III ongoing.	Treatment with immunosuppressive or cytotoxic drugs or use of anticancer CT or RT within the preceding 36 months.	No demographic data published or posted on ClinicalTrials.gov.
CVnCoV (lipid nanoparticle-mRNA)	CureVac	Two repeated i.m. doses	NCT04652102 EudraCT-2020-004066-19 Phase III ongoing.	Current diagnosis of or treatment of cancer.	No demographic data published or posted on ClinicalTrials.gov.
AG0302-COVID19	AnGes/Osaka University/Takara Bio	Two repeated i.m. doses	NCT04655625 Phase III ongoing.	Drugs that affect the immune system such as DMARDs, immunosuppressants, biologics.	No demographic data published or posted on ClinicalTrials.gov.
ZF2001 (protein subunits)	Anhui Zhifei Longcom/ Chinese Academy of Medical Sciences	Adjuvant + spike protein RBD; two repeated i.m. doses	NCT04646590 Phase III ongoing.	Cancer patients (except basal cell carcinoma).	No demographic data published or posted on ClinicalTrials.gov.
SCB-2019	Clover Biopharmaceuticals/ The Coalition for Epidemic Preparedness	AS03-adjuvated recombinant trimeric S-protein; two repeated i.m. doses	NCT04672395 Phase III ongoing.	Treatment with immunosuppressive therapy (cytotoxic agents, systemic corticosteroids) or planned receipt during the study period; history of malignancy within 1 year before screening.	No demographic data published or posted on ClinicalTrials.gov.
Vero cell (inactivated)	Chinese Academy of Medical Sciences	Two repeated i.m. doses	NCT04659239 Phase III ongoing.	History of malignant tumors.	No demographic data published or posted on ClinicalTrials.gov.
BCG	Murdoch Children's Research Institute	BCG	NCT04327206 (BRACE) Phase III ongoing.	History of any malignant tumors.	n.a.

All Covid-19 vaccine phase III trials ongoing are reported with details about cancer patient eligibility.[3]

Abs, antibodies; Ad, adenovirus; BCG, Bacillus Calmette-Guérin; COVID, coronavirus disease; CT, chemotherapy; DMARDs, disease-modifying antirheumatic drugs; EMA, European Medical Agency; EU, European Union; FDA, Food and Drug Administration; GSK, GlaxoSmithKline; i.m., intramuscular; mRNA, messenger RNA; n.a., not applicable; NIAID, National Institute of Allergy and Infectious Diseases; RBD, receptor-binding domain; RT, radiotherapy; S protein, spike protein; UAE, United Arab Emirates; VLP, virus-like particles.