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.

immediate referral area. Thus, the study population is representative of the general population of Israeli patients with cancer on active treatment.

Our presented data suggest a high rate of waning immunogenicity in patients with cancer approximately 6 months after the administration of the second dose of BNT162b2, and support the use of a booster dose in this vulnerable population of actively treated patients with cancer. The modest side-effect profile further supports this recommendation. Although the study cohort was relatively small, we believe that the explicit data from this population, combined with the robustness of the national data,[5] support the recommendation for a third dose booster for actively treated patients with cancer. YA declares receiving research grants from Pfizer, outside the scope of this work. AS is partially supported by the Israeli Council for Higher Education via the Weizmann Data Science Research Center, and by a research grant from the Estate of Tully and Michele Plesser. IW reports speaker fees and fees for consultancy from Roche, Bristol Myers Squibb, Merck Sharp & Dohme, Beyond Air, AstraZeneca, and Novartis; contracts or research funding from Roche, Novatis, Beyond Air, and Merck Sharp & Dohme; participation on a data safety monitoring board or advisory board of Merck Sharp & Dohme and AstraZeneca; participation in committee of Israeli Cancer Association; and stock options in Breath of life. All other authors declare no competing interests. COVI3 study investigators are listed at the appendix (p 4).

Hagai Ligumsky, Herut Dor, Tal Etan, Inbal Golomb, Alla Nikolaevski-Berlin, Inbal Greenberg, Tamar Halperin, Yoel Angel, Oryan Henig, Avishay Spitzer, Marina Slobodkin, Ido Wolf, in collaboration with the COVI3 study investigators

hagail@tlvmc.gov.il

Oncology Division (HL, TE, IGo, AN-B, AS, IW), Human Immunodeficiency Virus Laboratory (TH), Department of Anasthesia, Pain and Intensive Care (YA), Department of Infectious Diseases and Infection Control (OH), and Department of Internal Medicine "D" (MS), Tel Aviv Sourasky Medical Center 6423906, Tel Aviv, Israel; Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (HL, HD, TE, IGo, IGr, YA, OH, AS, MS, IW); Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel (AS)

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Safety of adjuvant CDK4/6 inhibitors during the COVID-19 pandemic

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During the COVID-19 pandemic, it was observed that patients with cancer who were undergoing treatment had an increased risk of contracting COVID-19, and a more severe course of infection, compared with individuals who did not have a history of cancer.[1] As this increased risk was not associated with more frequent exposure to health-care systems, it was thought to reflect a weakened immune system caused by the disease itself or anticancer treatment.[2]

Endocrine therapy, a highly effective and well-tolerated breast cancer therapy, is the mainstay of treatment for about two-thirds of patients with breast cancer. In the metastatic setting, the addition of cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitors has led to substantial improvements in progression-free survival and overall survival in first-line and pre-treated settings.[3,4] The side-effects of CDK4/6 inhibitors are generally manageable, but about 60% of patients might develop grade 3 or 4 neutropenia.[5] However, because this neutropenia is a consequence of cell cycle arrest (rather than cell death as with cytotoxic chemotherapy), it is reversible by pausing therapy for a few days. This side-effect is usually not associated with febrile neutropenia or serious infections, in contrast to what is seen with chemotherapy-induced neutropenia.[6]

Early in the COVID-19 pandemic, a guidelines manuscript suggested caution regarding the use of potentially immunosuppressive cancer therapies, including CDK4/6 inhibitors.[7,8] These guidelines might have led to reduced usage of CDK4/6 inhibitors in patients with breast cancer, potentially negatively affecting disease progression and survival.

In 2021, Erica L Mayer and colleagues,[9] reported an interim analysis in *The Lancet Oncology* of the

ongoing, global, phase 3 PALLAS trial, with the updated preplanned final analysis published in December, 2021.[10] Between Sept 1, 2015, and Nov 30, 2018, 5761 patients with early-stage breast cancer were randomly assigned (1:1) at 406 cancer centres in 21 countries to receive either 2 years of the CDK4/6 inhibitor palbociclib in addition to standard adjuvant endocrine therapy (n=2884) or adjuvant endocrine therapy alone (n=2877).[10] 2841 patients received palbociclib plus endocrine therapy and 2901 patients received endocrine therapy only; 36 individuals were excluded. The safety analysis of the PALLAS trial showed no new signals of adverse events for palbociclib, with grade 3–4 neutropenia being the most prevalent (in 1742 [61·3%] of 2840 patients on palbociclib and endocrine therapy *vs* 11 [0·3%] of 2903 on endocrine therapy alone).[9] Grade 3–4 upper respiratory tract infections occurred in 32 [1·1%] patients receiving palbociclib plus endocrine therapy and in three (0·1%) patients receiving endocrine treatment alone; these infections occurred at a consistent rate over the course of the trial.[9]

Given the absence of data describing the safety of CDK4/6 inhibitors during the COVID-19 pandemic, the PALLAS leadership conducted a risk–benefit assessment in March, 2020, of the safety of continuing palbociclib during the COVID-19 pandemic. It was decided by the PALLAS trial chairs and executive committee that palbociclib would not need to be paused for patients without symptoms indicative of COVID-19, with individual risk factors always being considered. This guidance was communicated in March 18, 2020, to all PALLAS site investigators via an internal study memo. In May, 2020, unique COVID-19 case report forms were introduced to the PALLAS study teams to capture information on COVID-19 testing, rates of infection, and outcomes. The testing method for COVID-19 was according to local care providers and was not mandated by the study.

As of Dec 1, 2019, of the 5761 patients who were randomly assigned and included in the intention-to-treat population,[10] 5125 (89·0%) remained on study (2552 [88·5%] of 2884 allocated to palbociclib plus endocrine therapy, of whom 847 [33·2%] were still receiving palbociclib, and 2573 [89·4%] of 2877 allocated to endocrine therapy alone). From Dec 1, 2019, to Nov 20, 2020, 721 (14·1%) of 5125 patients were tested for COVID-19 (test type not mandated, 362 [14·2%] of 2552 in the palbociclib group and 359 [14·0%] of 2573 in the endocrine therapy only group). Of the 721 tested individuals, 88 (12·2%) were positive for COVID-19, with no clinically meaningful difference in infection rate by study group (41 [11·3%] of 362 patients tested were positive in the palbociclib group *vs* 47 [13·1%] of 359 in the endocrine therapy only group). Of the 88 patients who tested positive for COVID-19, 57 (64·8%) reported symptomatic infections (28 [68·3%] in the palbociclib group and 29 [61·7%] in the endocrine therapy only group). No patient stopped endocrine therapy due to COVID-19-related reasons, whereas 27 (1·1%) of 2552 patients ended palbociclib therapy early due to an undefined COVID-19-related reason. One patient in the palbociclib plus endocrine therapy group and two patients in the endocrine therapy only group died due to COVID-19. Only four patients overall withdrew study consent for COVID-19-related reasons. As no COVID-19 vaccination programme was active during the data collection timeframe, the impact of vaccination on the rates of infection could not be addressed in this investigation, but could be considered in a future analysis. Additionally, rates of seroconversion after infection were not measured as part of this study; therefore, the impact of ongoing palbociclib or endocrine therapy on rates of seroconversion could not be determined.

In summary, in this updated analysis of the phase 3 PALLAS trial, reported rates of COVID-19 were low, with no differences in test positivity or symptomatic infection between patients receiving palbociclib plus endocrine therapy compared with those receiving endocrine therapy alone. These data provide reassurance about the safety of using palbociclib in breast cancer treatment during the COVID-19 pandemic.

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*Georg Pfeiler, Angela DeMichele, Amylou C Dueck, Christian Fesl, Michael Gnant, *Erica L Mayer*
erica_mayer@dfci.harvard.edu

Department of Gynecology (GP), Comprehensive Cancer Center (MG), Medical University of Vienna, Vienna, Austria; Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA (AD); Alliance Statistics and Data Center, Mayo Clinic, Phoenix, AZ, USA (ACD); Austrian Breast and Colorectal Cancer Study Group, Vienna, Austria (CF); Breast Oncology Center, Dana-Farber Cancer Institute, Boston, MA 02215, USA (ELM)

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Japan resumes active recommendations of HPV vaccine after 8·5 years of suspension

On Nov 26, 2021, the Ministry of Health, Labour, and Welfare of Japan officially issued an announcement to resume active recommendations of the human papillomavirus (HPV) vaccine, which had been suspended since June, 2013.[1] The new announcement now clearly advises municipalities to recommend the vaccine in accordance with Article 8 of the National Immunization Law, which includes sending notifications and vouchers individually to the target population (ie, girls aged 12–16 years).[1] Municipalities are expected to restart such active recommendations from April, 2022.

Even during the period when active recommendations were suspended, the HPV vaccine was maintained as a part of the national immunisation programme and provided free to girls in the target population seeking vaccination.[2] However, the target girls were not individually notified that they could have the vaccine. This situation continued despite large-scale epidemiological studies showing the effectiveness and safety of the vaccine in Japan and worldwide, and the scientific community repeatedly calling for the resumption of active recommendations by the Japanese government.[3–5] As a result, public resistance regarding the HPV vaccine in Japan has remained, and vaccination coverage stagnated at a low rate (<1%) over the past 7 years.

The new announcement provides four directions for municipalities in promoting HPV vaccination.[1] First, to pay careful attention to girls reaching the age of 16 years (the final age of the target population) in any fiscal year between 2022 and 2024. Second, to secure sufficient consultation and medical care systems for people who might have adverse effects after vaccination, in collaboration with the local health facilities, medical associations, and other relevant parties. Third, to ensure enough information about the efficacy and safety of the HPV vaccine is provided at local health facilities for girls who wish to be vaccinated. Fourth, to ensure all suspected adverse reactions to the HPV vaccine are reported appropriately. With regard to catch-up vaccinations for girls who missed the opportunity during the suspension, the Ministry informed municipalities of the Health Science Council's recommendation on providing the vaccine at public expense to girls born between 1997 and 2005 (ie, girls aged 17–25 years in 2022) over the next 3 years.

Cervical cancer has become a global health agenda, with WHO member states adopting the global strategy to accelerate the elimination of cervical cancer in 2020.[6] Efforts are underway in many countries to introduce and scale-up HPV vaccination, and meet the target of 90% of girls being fully vaccinated with the HPV vaccine by the age of 15 years by 2030. As of December, 2021, 116 countries (60% of WHO member states) have introduced the vaccine into their national immunisation programme, and some countries, such as Norway, Mexico, and Rwanda, have already proven