Methods

Study population

Memorial Sloan Kettering Cancer Center (MSKCC) located in New York City is a 574-bed tertiary cancer center with approximately 25,000 annual admissions. From January 1, 2022, to July 31, 2022, all consecutive patients >=12 years of age weighing at least 40 kg who received AZD7442 were included in the study. A retrospective analysis of 892 AZD7442 recipients was conducted. Identification of case patients and their medical background and clinical course from COVID-19 were extracted from the electronic medical record. Chronic infection from COVID-19 was defined as progressive or recurrent COVID-19-related symptoms in the absence of alternative explanation and with or without evidence of viral persistence. The MSKCC Institutional Review Board granted a Health Insurance Portability and Accountability Act waiver of authorization to conduct this study.

Laboratory methods

SARS-CoV-2 RNA test

Viral RNA was detected using nasopharyngeal swabs (NPS) or saliva samples as previously described. [16] Briefly, SARS-CoV-2 RNA was tested for by real-time reverse transcription-polymerase chain reaction (RT-PCR) using several commercial assays. These included the Cobas® SARS-CoV-2 test (Roche Molecular Diagnostics, Indianapolis, Indiana USA), the TaqPath™ COVID-19 Combo Kit (Thermo Fisher Scientific, Waltham, MA), the ePlex Respiratory Panel 2 (GenMark/Roche Molecular Diagnostics, Indianapolis, IN), and the BioFire Respiratory Panel 2.1 (BioMerieux, Salt Lake City, UT). Samples were reported as positive per the manufacturers' instructions.

Anti-SARS-CoV-2 spike IgG antibody assay was performed as previously described. [17]

SARS-CoV-2 whole genome sequencing

Whole genome sequencing (WGS) was performed on samples with a cycle threshold (Ct) value <30 to increase likelihood of successful sequencing. Samples from platforms that do not provide a Ct value (i.e., BioFire RP 2.1 and ePlex 2) underwent WGS without knowledge of Ct value. WGS was performed as previously described using the ARTIC protocol with version 4.1 primers (Integrated DNA Technologies [IDT (Integrated DNA Technologies)], Coralville, Iowa USA) [18]. Pangolin software (https://github.com/cov-lineages/pangolin) was used to assign lineages for each consensus sequence using the Pango nomenclature.

Statistical analysis

Baseline demographic and clinical characteristics for all study patients were reported as absolute frequency and percentage or median with interquartile range (IQR), as appropriate. The FDA revised dosing recommendations several times since the original EUA. [15] Due to revised guidance from the FDA on AZD7442 dosing, study patients received varied dosing during the evaluation period. Therefore, we classified our study patients into four groups based on the dosage of AZD7442 they received. Patients who received one dose of 150 mg of both medications were in the "1 dose 150 mg/150 mg" group (dose group 1); those who received subsequent doses of 150 mg over the course of the study period were in the "2 doses 150 mg/150 mg" group (dose group 2); those who received one dose of 150 mg of both medications and then 300 mg doses on a later date were in the "1 dose 150 mg/150 mg and 1 dose 300 mg/300 mg" group (dose group 3); and lastly, those who received only one dose of 300 mg of both medications were in the "1 dose 300 mg/300 mg" group (dose group 4).

Crude estimates of treatment effect were stratified by dose groups. The number of breakthrough infections, total number of person-days, and incidence rate per 1000 person-days for each stratum were calculated. Follow-up person-days began from the initial date of AZD7442 administration until the SARS CoV-2 breakthrough date, death, or the end of the study period (31 July 2022). Incidence rate ratios (95% confidence interval) were calculated to assess the association between breakthrough infection by dose group.

To examine the relationship between breakthrough infection and AZD7442 dosage, we performed extended Cox regression analyses using a counting process data structure to account for the varying dosages of AZD7442 administered at different time periods. In this approach, start and stop times of each patient observation defined intervals during which AZD7442 dosage remained constant. Dose group was defined as the primary time-varying exposure variable and breakthrough infection as the outcome of interest with death as a competing risk. Because missing data pattern was randomly dispersed throughout the dataset (i.e., missing completely at random), listwise deletion was used to exclude any records for which variables were missing.

For each dose group, univariable Cox regression analyses were performed to evaluate potential risk factors for breakthrough infection. Results were expressed as hazard ratios (HR) and the corresponding 95% confidence intervals. Variables that were significant at $p<0.05$ in the univariable analysis were considered for the multivariable cox regression model. Due to the small number of breakthrough infections for patients in dose group 3, model estimates for this group were not reported.

All statistical analyses were performed using SAS version 9.4 software (SAS Institute Inc., Cary, NC).