Clinical Efficacy of AZD7442 (Tixagevimab/Cilgavimab) as Prophylaxis Against SARS-CoV-2 Infection in Immunosuppressed Cancer Patients (EIMPRIS Study)

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ABSTRACT:

Introduction:

There remains a need for prevention of symptomatic SARS-CoV-2 infection in patients with cancer at increased risk for COVID-19 morbidity. We assessed clinical efficacy of AZD7442, a combination of two long-acting monoclonal antibodies, for prevention of symptomatic infection.

Methods:

The trial enrolled previously-vaccinated cancer patients at 40 community-based medical practices. Patients received one dose of AZD7442 600 mg IM/IV. A subset received a second dose at 180 days. Assessments included blood draws for AZD7442 serum concentrations, receptor binding domain (RBD)-IgG antibody levels and T cell analyses. Measurements of T cell activity were based on Polyfunctional Strength Index (PSI). RT-PCR tests were used to assess for infection in symptomatic patients. Quality of Life (QoL) was assessed using the FACT-G7 questionnaire.

Results:

550 patients (mean age, 68.1 y; 50.7% female; 83.8% White/Caucasian; hematologic malignancy, 44.7%; solid tumor, 54.0%; both, 1.3%) were enrolled from June 2022 to February 2023. There were 66 SARS-CoV-2 positive symptomatic events in 64 patients. Time between AZD7442 administration and positive SARS-CoV-2 test result was 92 days. No SARS-CoV-2-related deaths occurred. Seven patients were hospitalized for SARS-CoV-2; none requiring supplemental oxygen or intubation. At Day 30, mean CD4+ T cell PSI was lower than in non-cancer controls while mean CD8+ PSI was higher (P=0.004 and P=0.017, respectively). Mean CD4/CD8 PSI values for SARS-CoV-2-infected patients were similar compared to same subjects at Day 30. At baseline, mean RBD-IgG for hematologic patients was significantly lower than for solid tumor patients (440 vs 650). Mean values at 3, 6, and 9 months were similar between the subgroups (range, 683–800). QoL scores did not change significantly over the study.

Conclusions:

AZD7442 appears to protect against SARS-CoV-2 symptomatic infection in cancer patients. SARS-CoV-2 hospitalizations did not require supplemental oxygen/intubation or result in death. Breakthrough symptomatic SARS-CoV-2 infections were low and comparable between AZD7442 treated solid tumor and hematologic patients.

Table 1. Baseline Data

Characteristics	All Patients N = 550	By Cancer Type: Hematologic Malignancy N=246[a]	By Cancer Type: Solid Tumor N=297[a]
Age	68.1 (11.2)	69.7 (11.5)	66.5 (10.9)
Min, max	23, 96		
Age Group, y			
≤50	39 (7.1)	12 (4.9)	27 9.1)
51-60	73 (13.3)	28 (11.4)	45 (15.2)
61-70	181 (32.9)	72 (29.3)	108 (36.4)
71-80	196 (35.6)	100 (40.7)	92 (31.0)
80+	61 (11.1)	34 (13.8)	25 (8.4)
Gender			
Female	279 (50.7)	99 (40.2)	180 (60.6)
Male	271 (49.3)	147 (59.8)	117 (39.4)
Race			
Non-Caucasian	89 (16.2)	36 (14.6)	52 (17.5)
White (or Caucasian)	461 (83.8)	210 (85.4)	245 (82.5)
Ethnicity			
Hispanic or Latino	27 (4.9)	11 (4.5)	16 (5.4)
Other	523 (95.1)	235 (95.5)	281 (94.6)
Height, inches	66.7 (4.2)	67.5 (4.0)	66.1 (4.3)
Weight, lb	174.3 (44.0)	175.7 (39.5)	173.1 (47.8)
BMI, kg/m²	27.5 (6.3)	27.1 (5.4)	27.8 (7.0)
Cancer Class			
Hematologic malignancy	246 (44.7)	246 (100.0)	0
Solid Tumor	297 (54.0)	0	297 (100.0)
Both	7 (1.3)	---[a]	---[a]
Treatment Category			
Chemotherapy	152 (27.6)	26 (10.6)	125 (42.1)
Immunotherapy	46 (8.4)	4 (1.6)	41 (13.8)
Targeted	241 (43.8)	183 (74.4)	54 (18.2)
Combo	108 (19.6)	30 (12.2)	77 (25.9)
None	3 (0.5)	3 (1.2)	0

Data are mean (SD) or n (%)

BMI, body mass index; lb, pounds; y, years

[a]Seven patients with both cancer types are not included in the demographic breakdown by cancer type

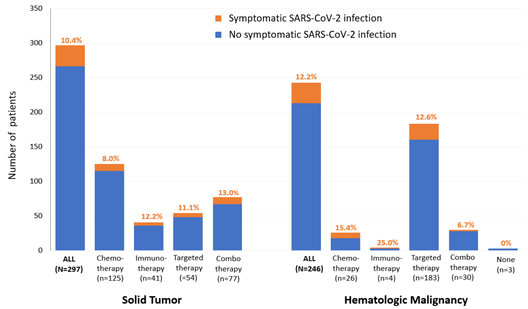

Figure 1. Distribution of symptomatic and RT-PCR+ SARS-C0V-2 positivity by cancer type and cancer therapy category. Bars represent numbers of patients. Percentages indicate the percentage of SARS-CoV-2+ patients within each subgroup (orange sub-bars).

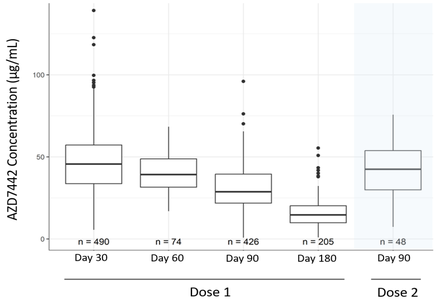

Figure 2. AZD7442 serum concentration over time in immunosuppressed cancer patients after first and second doses. Lines represent medians; boxes represent 1st and 3rd quartiles; whiskers extend from the upper/lower quartiles to the largest/smallest values (respectively) no further than 1.5x the upper/lower quartile; data beyond the ends of the whiskers are outliers and plotted individually.

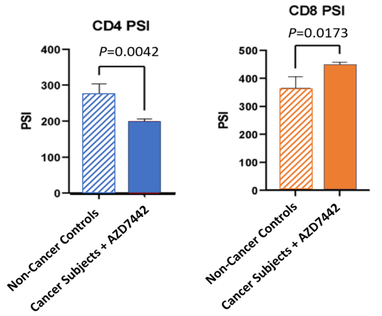

Figure 3. Averaged Polyfunctional Strength Index (PSI) for CD4+ and CD8+ cells for cancer patients administered the monoclonal antibody combination AZD7442 (Day 30 post-treatment; N=505) versus control (non-cancer) donors stimulated with PMA/Iono (N=50)

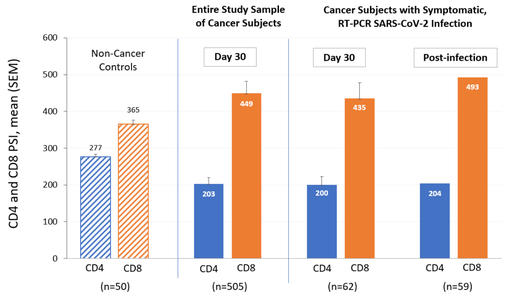

Figure 4. Averaged Polyfunctional Strength Index (PSI) for CD4+ and CD8+ cells for cancer patients administered the monoclonal antibody combination AZD7442 who were symptomatic and RT-PCR+ for SARS-CoV-2; values shown for Day 30 post-AZD7442 administration and post-symptomatic SARS-CoV-2 infection, compared to non-cancer controls.

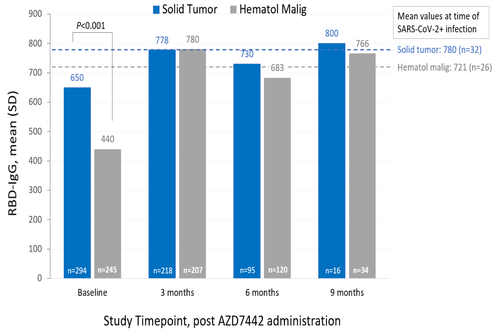

Figure 5. Mean RBD-IgG values by cancer type for all study assessments and mean values at time of SARS-CoV-2 infection.

CONCLUSIONS:

- The EIMPRIS trial demonstrated that AZD7442 monoclonal antibody is safe, tolerable, and effective in preventing symptomatic SARS-CoV-2 infection among cancer patients.
- Findings highlight the critical interaction between B cells and T cells in high-risk cancer patients' immune response to SARS-CoV-2.
- Evidence from the study indicates that patients with hematologic malignancies often exhibit inadequate immune responses to vaccines, necessitating alternative protective measures.
- AZD7442 administration significantly enhanced immune cell responses and provided substantial protection against severe COVID-19 outcomes in the studied patient population.
- The study advocates for further research into monoclonal antibody therapies as a preventive strategy in community-based medical settings during SARS-CoV-2 and future viral pandemics.

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