

Staggered Schedule of Chemo-Immunotherapy (Durvalumab, Carboplatin and Pemetrexed) for Metastatic, Non-Squamous, NSCLC

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INTRODUCTION

The optimal sequencing of immune checkpoint blockade and chemotherapy remains uncertain. Preclinical and translational data demonstrate that chemotherapy alters tumor antigen release and immune microenvironment. We conducted STAGGER: a randomized, Phase II trial to determine if sequencing of ICI and chemotherapy affects the clinical benefit rate. We also evaluated correlatives including lymphocyte subsets and patient-reported outcomes.

METHODS

43 patients with metastatic non-squamous NSCLC were randomly assigned to treatment with durvalumab, carboplatin/pemetrexed.

As demonstrated in the study schema, for cycles 1-2, Arm A received durvalumab 1 week before chemo, and Arm B did the reverse. Cycles 3 and 4 were given on the same days and were followed by maintenance pemetrexed/durvalumab for 2 years. The trial was closed early due to limited accrual.

Correlative studies included analysis of peripheral blood lymphocyte subsets by flow cytometry at timepoints including screening, C2D1 and EOT, patient reported outcomes (PROs), and activity metrics by FitBit monitoring.

Here we present the final PFS and OS data as well as analysis of statistically significant lymphocyte subset changes.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

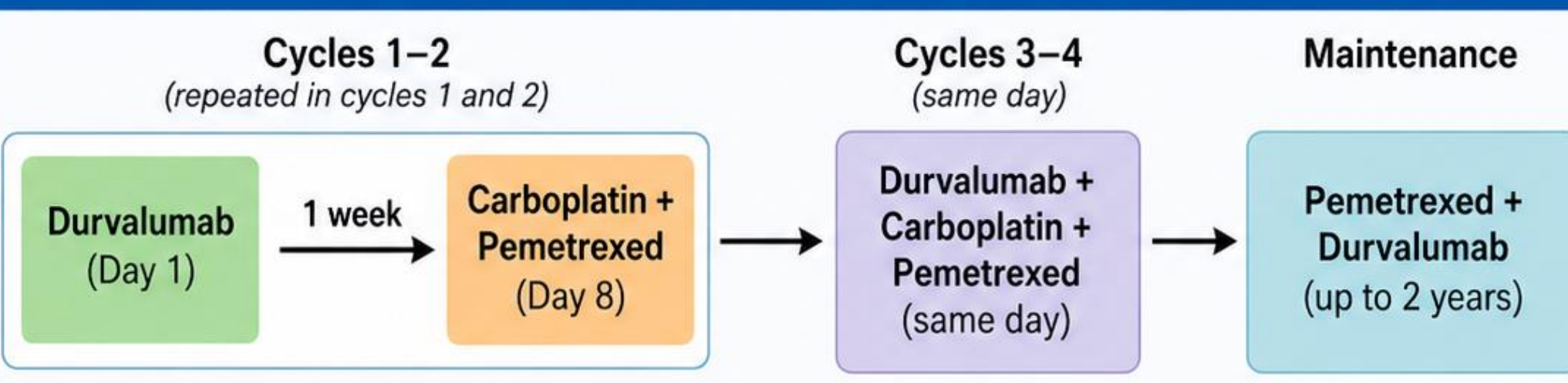
- Concurrent chemoimmunotherapy with durvalumab, carboplatin and pemetrexed given in a staggered schedule is an effective treatment for Non-Sq, NSCLC with long-term survival and minimal toxicity.
- The sequencing of concurrent chemo and immunotherapy for the first 2 cycles does not appear to affect overall survival.

Future Direction for Research

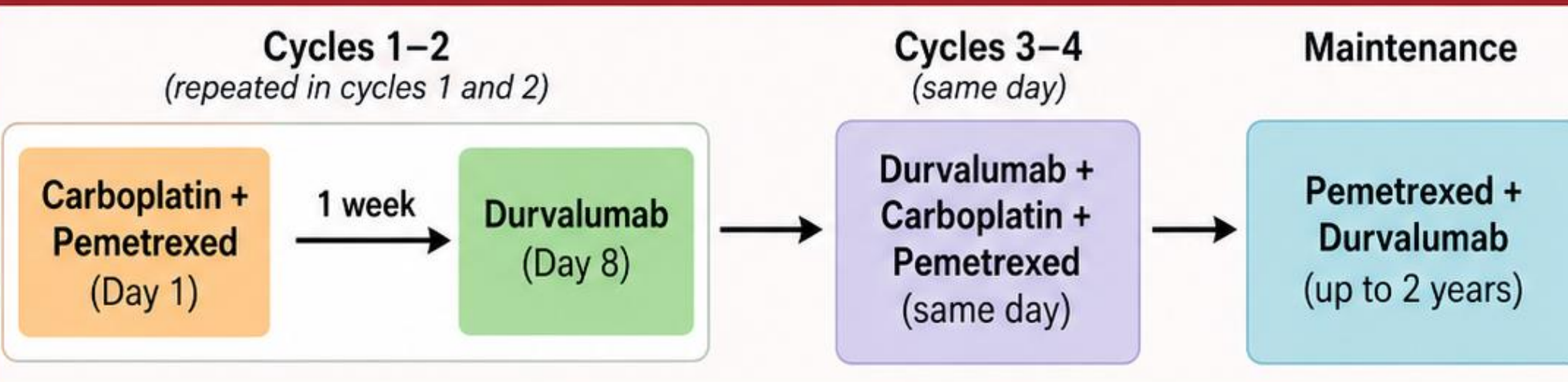
- Correlative analysis including PROs ongoing

STUDY SCHEMA

Arm A: Durvalumab before chemotherapy



Arm B: Chemotherapy before durvalumab



REFERENCES & ACKNOWLEDGEMENTS

We would like to acknowledge, most importantly, the patients who participated in this trial, and their families. We thank AstraZeneca for support of this trial. Finally, we thank LCRF for funding to MG and VAMC and DOD for funding to SBP.

ChatGPT and Claude were used to assist with figure making but not in data analysis (STATA, R, and Prism were used for data analysis)

RESULTS

A Progression Free Survival

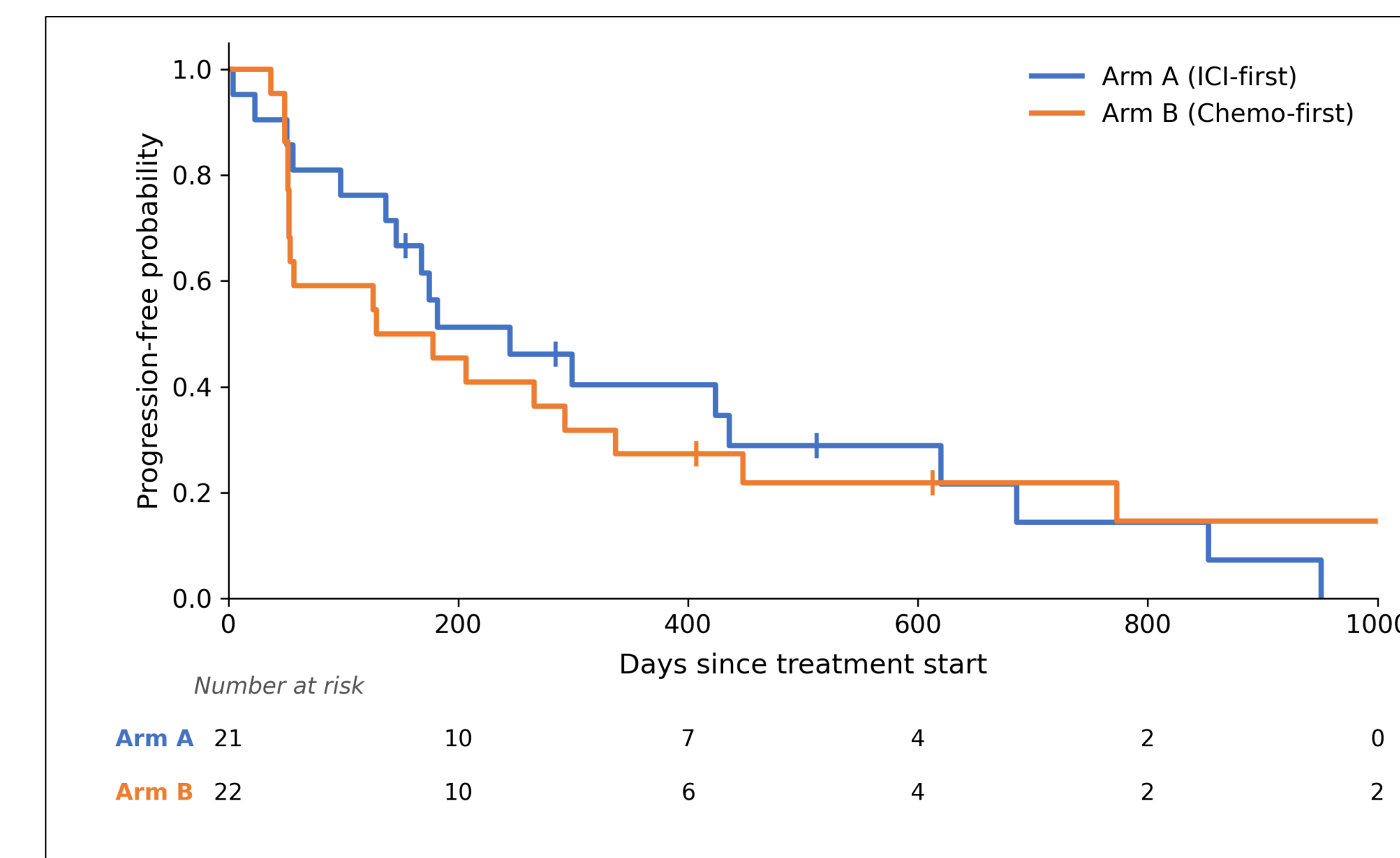


Figure 1. Kaplan-Meier estimate of progression-free survival by treatment arm amongst the intention-to-treat (ITT) population. PFS is the earlier of documented disease progression by RECIST 1.1 or death, patients were censored (tick marks) at last contact if neither occurred. Median PFS: Arm A 182 days, Arm B 153.5 days (log-rank $p=0.87$).

B Clinical Benefit Rate

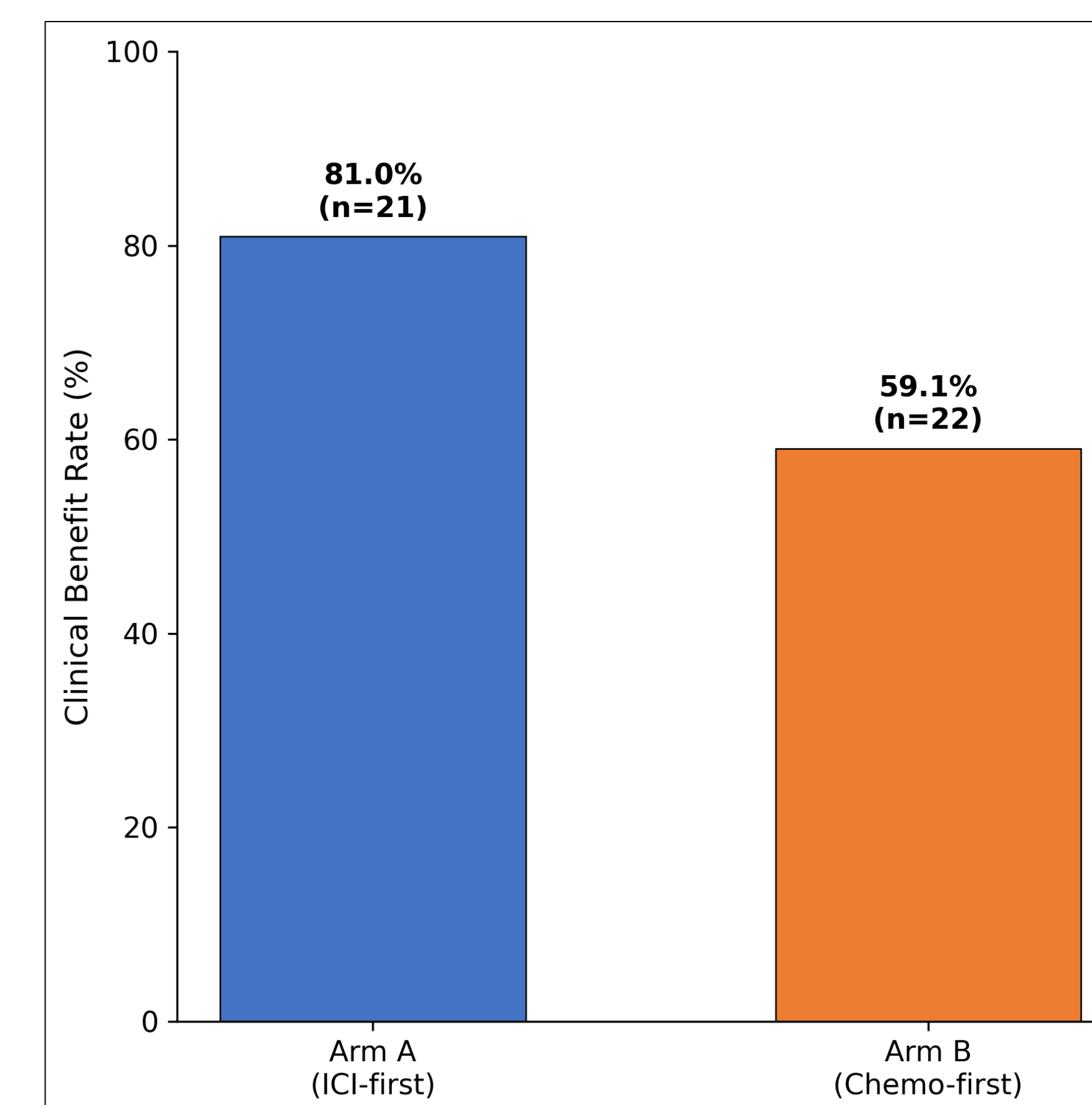


Figure 2. Clinical benefit rate by RECIST-confirmed response data. CBR defined as the proportion of patients who ever achieved disease control (stable disease, partial response, or complete response) at any evaluation during treatment. (chi-square $p=0.12$).

C Overall Survival

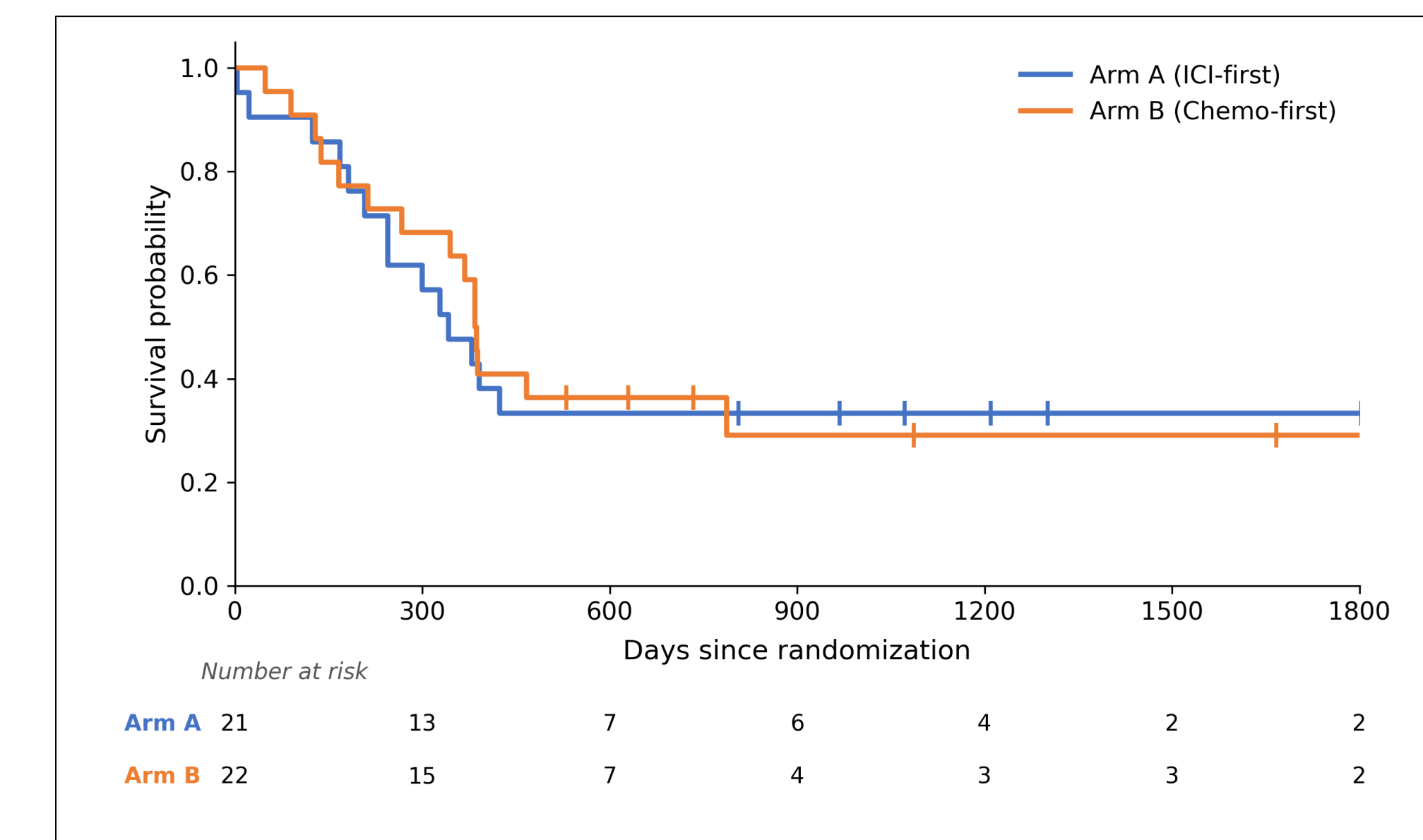


Figure 3. Kaplan-Meier estimate of overall survival by treatment arm amongst the ITT population. Arm A received durvalumab one week before carboplatin/pemetrexed in cycles 1–2; Arm B received chemotherapy first. Curves are censored at last contact (administrative censoring at trial closure) and extend to each arm's longest observed follow-up. Median OS: Arm A 342 days, Arm B 385.5 days (log-rank $p=0.97$).

D Lower T cells at C2D1 in Arm A

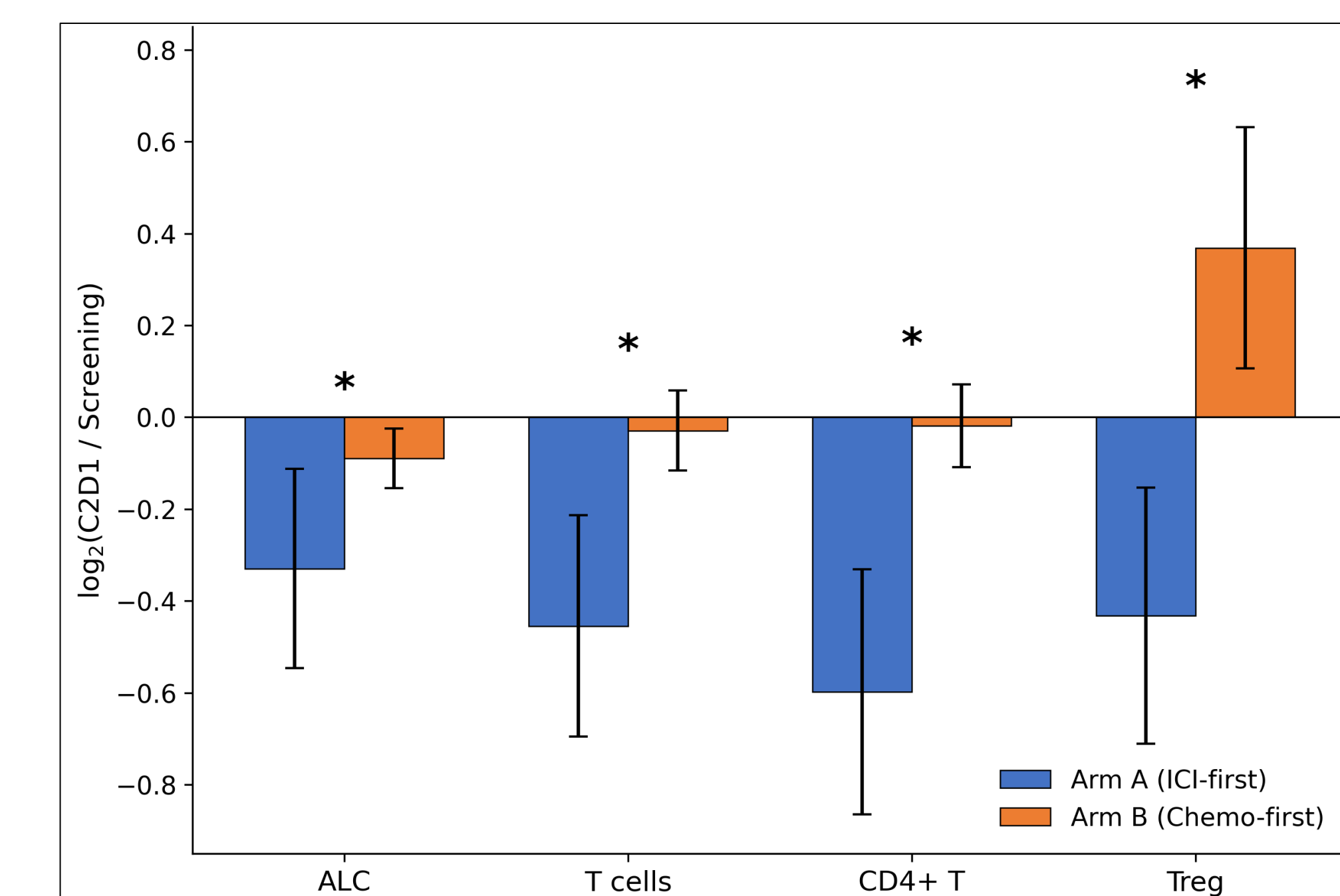


Figure 4. Patients in Arm A had significantly decreased absolute numbers of peripheral blood lymphocytes (ALC), CD3⁺ T cells, CD4⁺ T cells, and regulatory T cells compared to baseline, unlike patients in Arm B. Baseline-normalized change in log-transformed absolute lymphocyte counts from Screening to C2D1 per patient (mean ± SEM shown); a value of 0 indicates no change from baseline. Arm A shows a significantly larger early contraction than Arm B in all four subsets shown. p -values were FDR-corrected for multiple comparisons. * $q<0.05$. No subset differed significantly between arms at EOT.