

P 2343: Time-Dependent Prognostic Impact of Distant Metastatic Sites in SCLC: A Comparison of Pre- and Post-Immunotherapy Eras



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INTRODUCTION

While immune checkpoint inhibitors (ICIs) have improved survival in extensive-stage small cell lung cancer (ES-SCLC), their organ-specific effects remain unclear. It is unknown whether ICIs have altered the established prognostic hierarchy of metastatic sites. This study aimed to evaluate the time-dependent prognostic impact of distant metastases in ES-SCLC across pre- and post-immunotherapy eras.

METHODS

Using the SEER Research Data (17 Registries, Nov 2024 Sub), we identified 43,279 patients with metastatic SCLC diagnosed between 2010-2022 (Figure 1). Patients were grouped into the pre-ICI (2010–2018) and ICI (2019–2022) eras, using the 2019 FDA approval of first-line atezolizumab plus chemotherapy as the temporal cutoff. The primary endpoint was overall survival (OS). Kaplan–Meier analysis and multivariable Cox regression were used to assess survival and independent prognostic factors. Time-dependent area under the curve (AUC) analysis estimated the cumulative/dynamic AUC of each metastatic site at monthly intervals up to 36 months. Interaction terms tested whether the prognostic effects of metastatic sites differed between treatment eras. Exploratory analyses were stratified by age, sex, and chemotherapy status.

Total 86,399 patients from Incidence - SEER Research Data, 17 Registries, Nov 2024 Sub (2000-2022) database

Excluded patients:
Diagnosed between 2000-2009 (n=5,971)
Age < 18 years (n=1)
Non-extensive-stage SCLC (n=28,169)
Unknown race (n=77)
Radiotherapy recommended, but unknown if administered (n=494)
Unknown status for bone, brain, liver, or lung metastases (n=3,446)
Unknown survival months (n=22)
Not the primary tumor by international rules (n=415)
M0 (non-metastatic) or M-Not Applicable status (n=4,525)

Final Study Cohort (n=43,279)

Figure 1. Flow diagram of patient selection.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- The prognostic landscape of ES-SCLC has selectively changed in the ICI era.
 - Liver metastasis remains the dominant adverse prognostic factor, with consistently high time-dependent discrimination across both eras.
 - The prognostic impact of brain metastasis was markedly attenuated in the ICI era, potentially reflecting advances in systemic therapy, intracranial radiotherapy, and surveillance.
 - Bone metastasis showed limited prognostic value in the absence of concurrent liver involvement, emphasizing the importance of metastatic patterns rather than individual sites alone.
- ### Future Direction for Research
- These findings support a more personalized and site-specific approach to risk stratification and treatment planning in modern ES-SCLC management.
 - Prospective validation using patient-level ICI exposure and molecular data is required.

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RESULTS

Overlap of Distant Metastasis Sites in SCLC Patients
Data from SEER Database (2010–2022)

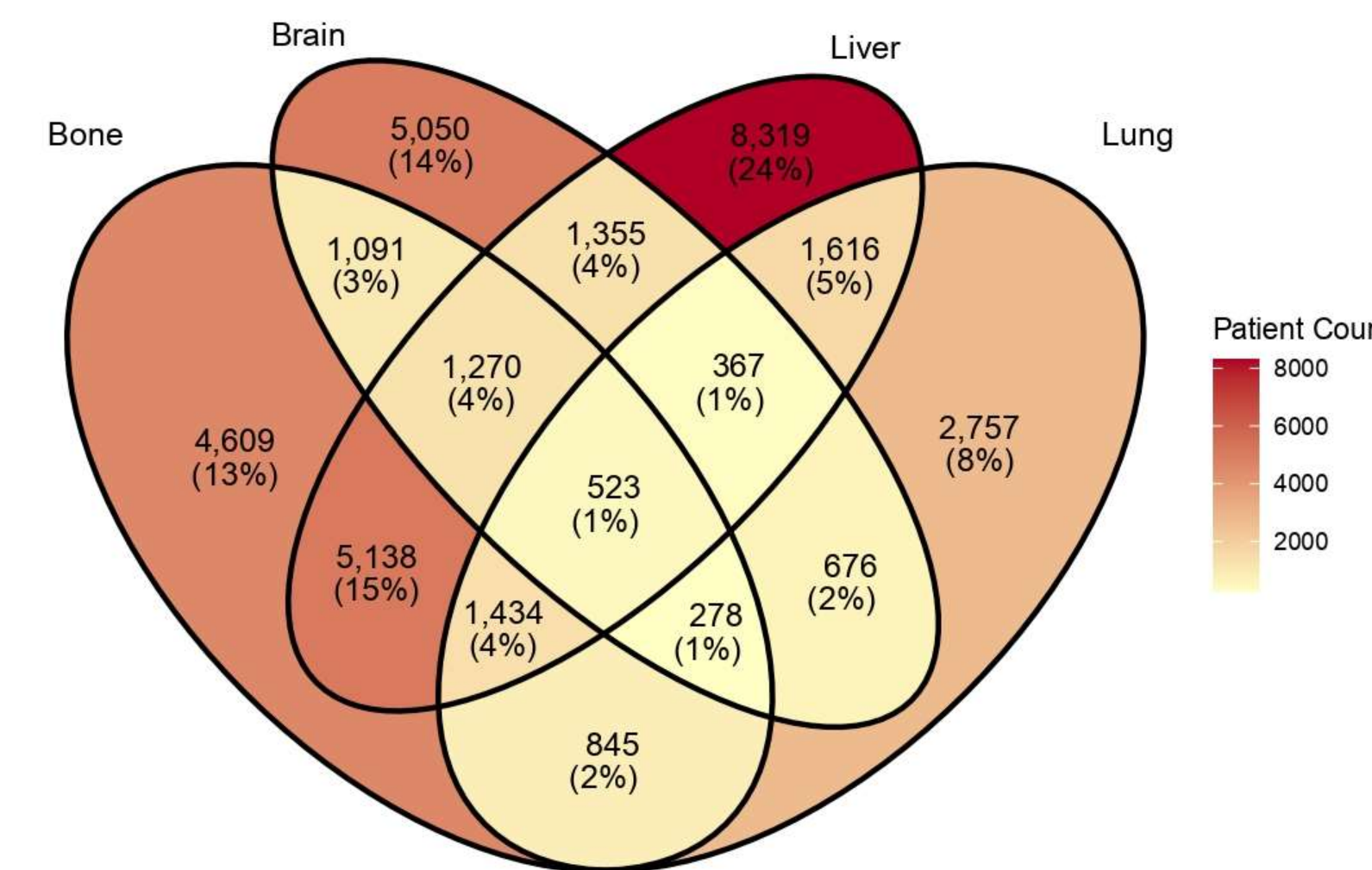


Figure 2. Venn diagram illustrating the overlap of distant metastasis sites in patients with ES-SCLC.

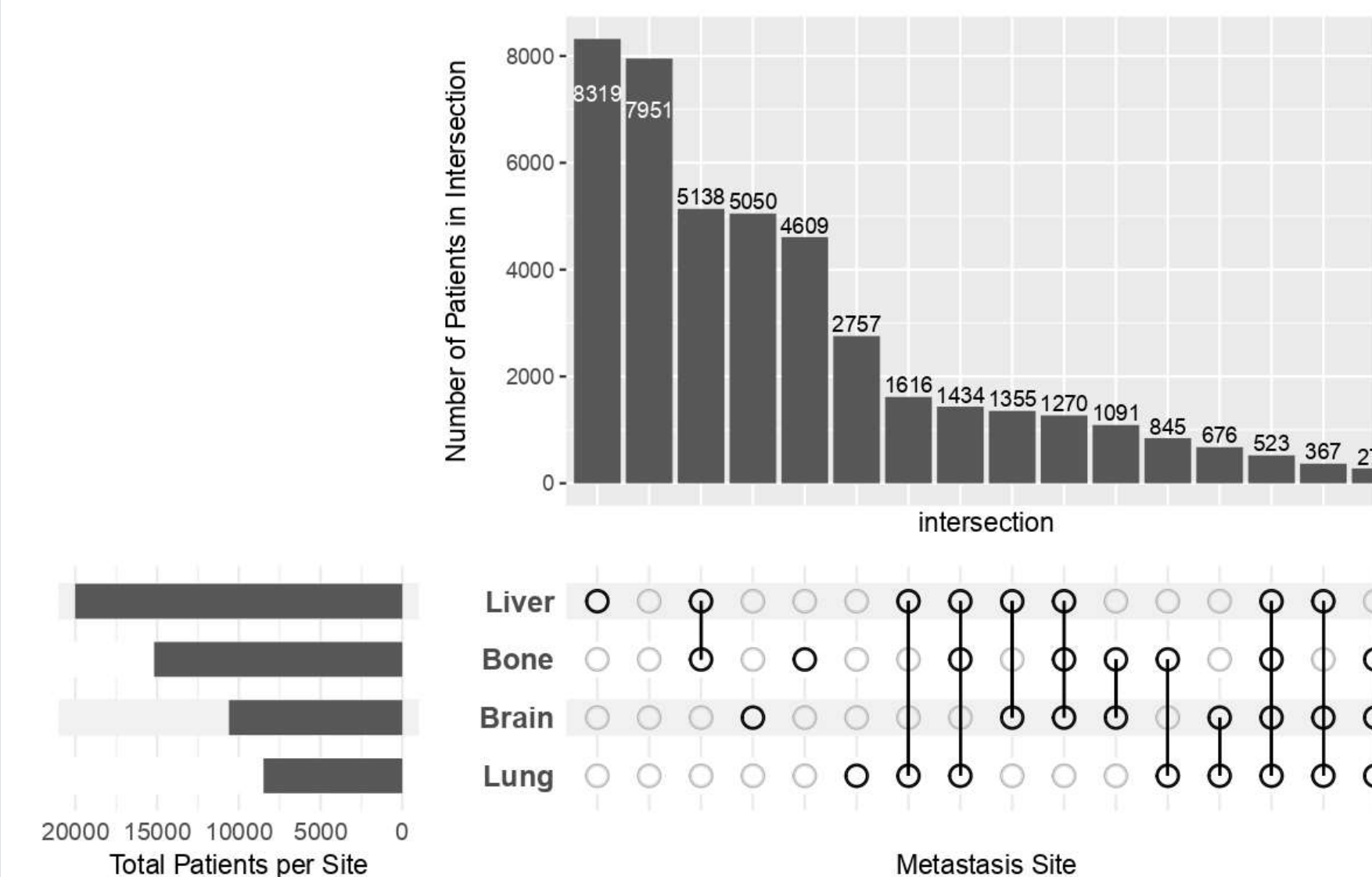


Figure 3. UpSet plot demonstrating the distribution and intersection of distant metastasis sites.

Time-dependent analysis demonstrated that liver metastasis had the highest and most persistent prognostic discrimination in both eras (mean AUC: 0.626 vs. 0.621; Figure 4A–B).

Conversely, the discriminatory value of brain metastasis decreased from 0.507 to 0.482, with a significant era-by-brain interaction (P-interaction=0.007). After excluding concurrent liver involvement, bone metastasis showed limited prognostic discrimination in both eras (mean AUC: 0.489 vs. 0.477; Figure 4C–D).

Among 43,279 patients, 70.8% were diagnosed in the pre-ICI era and 29.2% in the ICI era. Liver was the most frequent metastatic site (46.3%), followed by bone (35.1%), brain (24.5%), and lung (19.6%). Among patients with at least one of these four coded sites, liver-only disease was the most frequent presentation (24%), while liver–bone involvement was the predominant two-site combination (15%). Among patients with three metastatic sites, the combination of liver, bone, and lung was the most common, affecting 1,434 patients (4%). Metastasis to all four sites (bone, brain, liver, and lung) was less frequent, occurring in 523 patients (1%) (Figures 2–3).

During a median follow-up of 70 months, 93.4% patients died. Median OS was 5.0 months in both eras; however, the OS distribution was improved in the ICI era (log-rank $p < 0.001$). A similar improvement was observed among chemo-treated patients despite identical median OS of 8.0 months. In multivariable analysis, all four metastatic sites were independently associated with worse OS. Liver involvement remained the strongest site-specific adverse factor (HR=1.44, 95% CI: 1.41–1.47; $p < 0.001$).

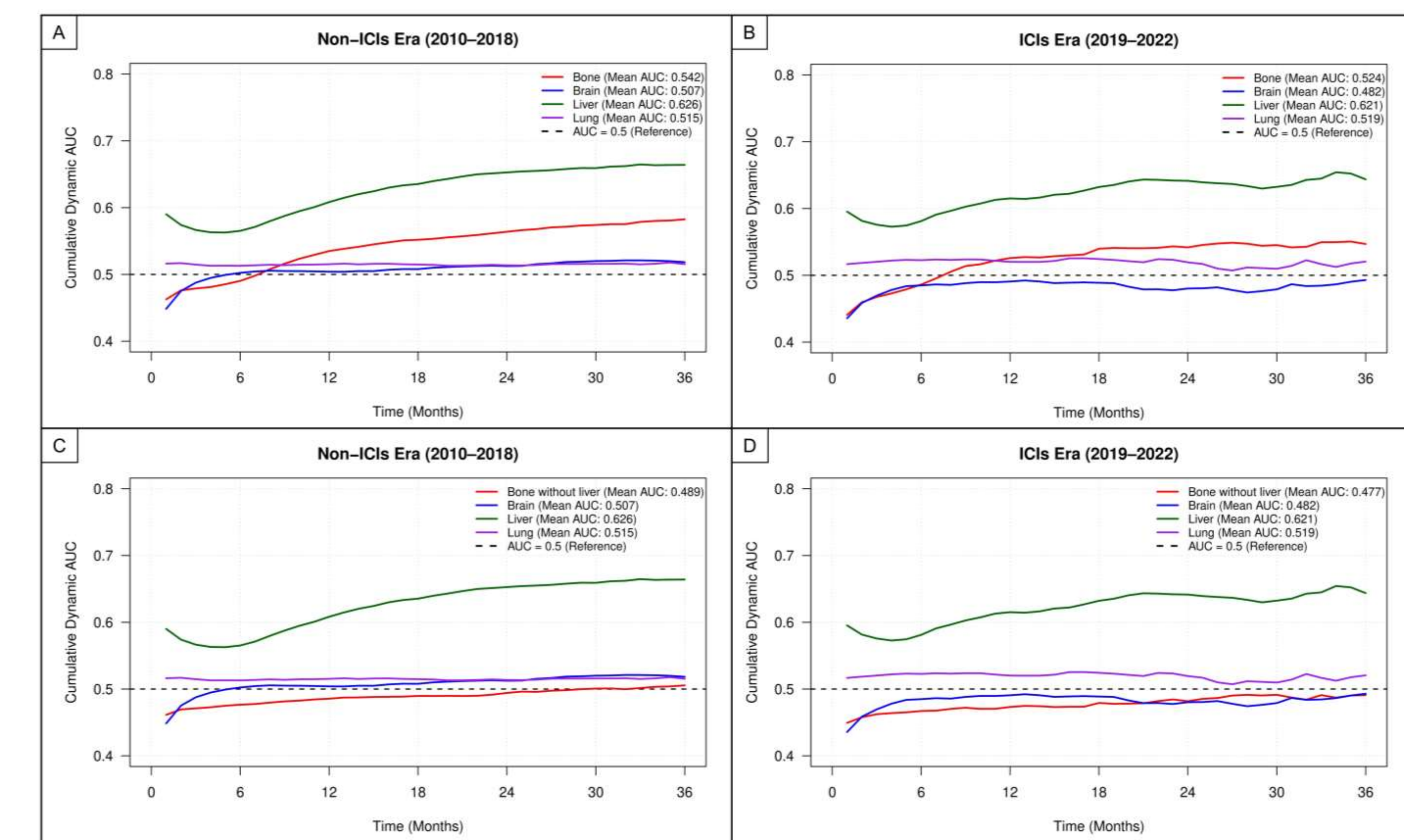


Figure 4. Time-dependent cumulative dynamic AUC curves for overall survival by metastatic site in metastatic SCLC. Panels (A) and (B) show the predictive performance of individual distant metastasis sites for overall survival in the non-ICI era and ICI era, respectively. Panels (C) and (D) depict the same analyses after excluding patients with concurrent bone and liver metastases ("bone without liver" subgroup).