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Spatial Co-occurrence Patterns of Immune-Related Adverse Events Associate with Anti-PD-(L)1 Efficacy in NSCLC

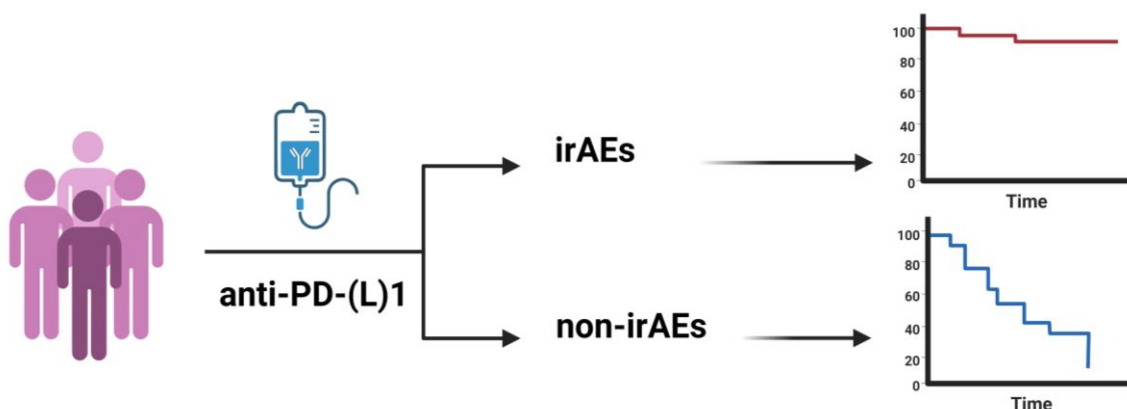
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Introduction

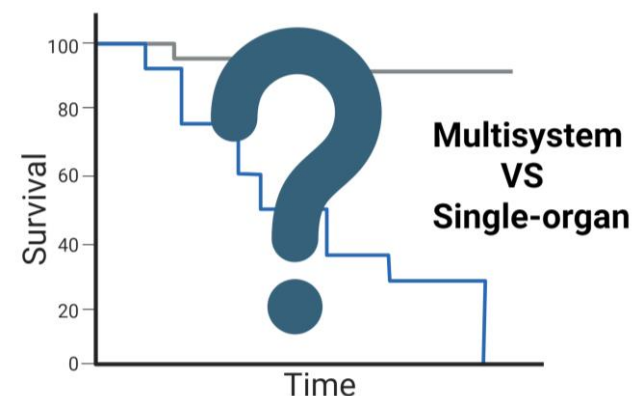
Background

- Immune-related adverse events (irAEs) are linked to improved survival with anti-PD-(L)1 therapy in NSCLC.
- It is unknown whether multisystem (≥ 2 organ systems) irAEs confer a different survival benefit compared with single-organ irAEs.
- Whether spatial co-occurrence patterns and organ distribution vary across treatment settings (adjuvant, first-line, second-line+) remains unclear.



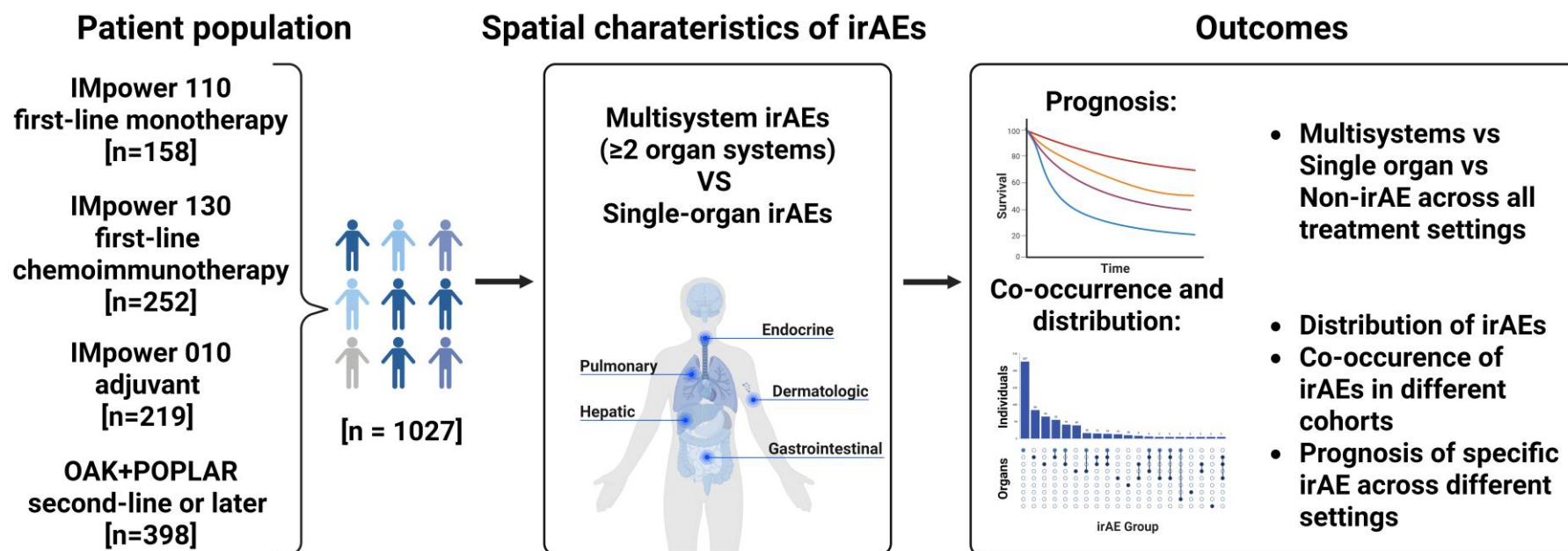
Objective

- To characterize irAE co-occurrence patterns and organ distribution, and assess their association with overall survival (OS) across different treatment settings in large pooled cohort.



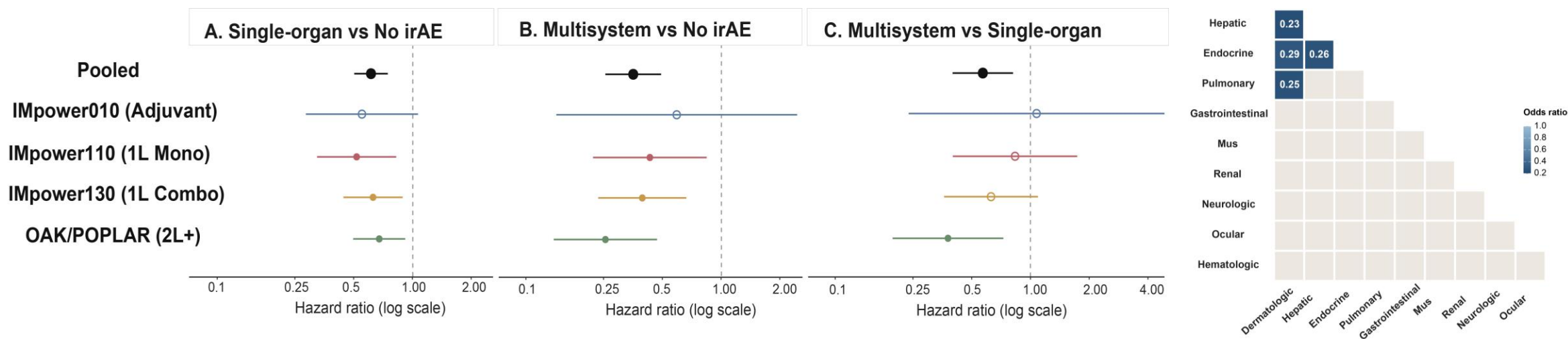
METHODS

- Integrating 1027 patients from 5 study cohorts and assigned patients to 4 treatment modalities.
- Prognostic and descriptive analysis of multisystem and single-organ irAEs.
- Analysis of organ-distribution and organ-specific survival analysis



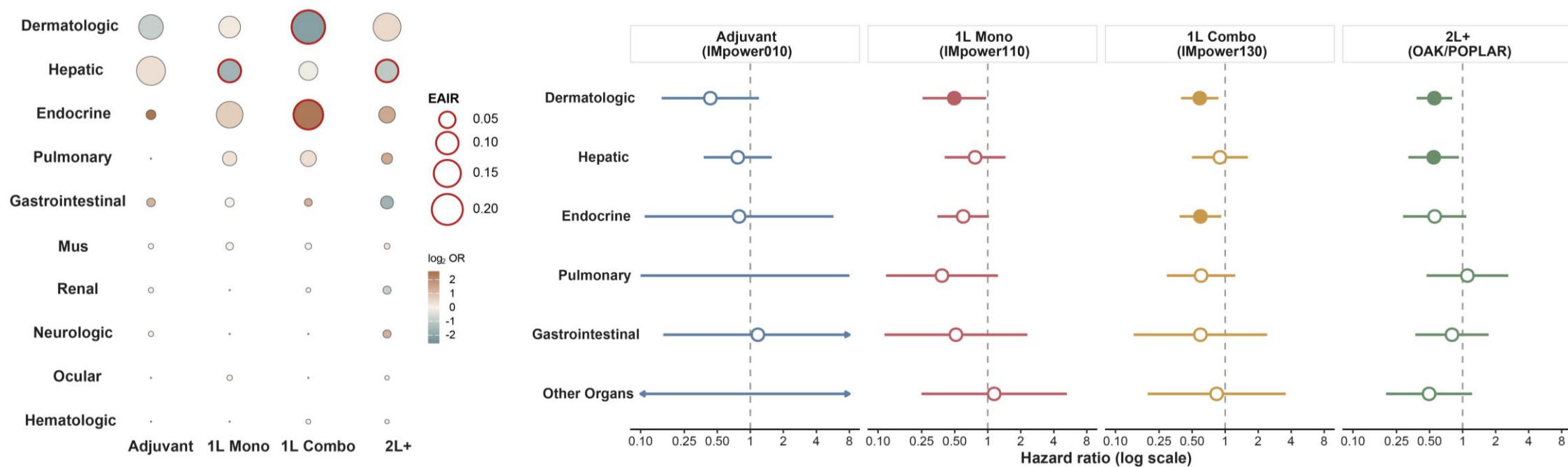
RESULTS

- **Pooled analysis:** Multisystem irAEs and single-organ irAEs both superior to no irAE.
- **Setting-specific:** Strongest in 2L+ cohort (HR 0.38, $p=0.004$); not observed in adjuvant cohort.
- **Four lower co-occurrence incidence rate paires:** Dermatologic-Endocrine, Dermatologic-Hepatic, Endocrine-Hepatic, Dermatologic-Pulmonary.



RESULTS

- **Organ distribution:** Differs by treatment settings.
- **Organ-specific survival benefit:** Dermatologic irAEs (advanced settings), endocrine irAEs (1L combo settings) and hepatic irAEs (2L+ settings)



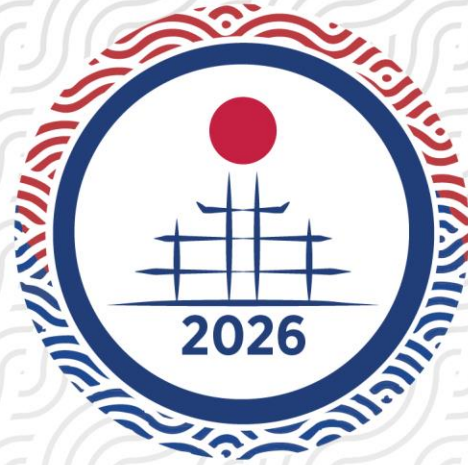
DISCUSSION AND CONCLUSION

DISCUSSION

- Multisystem irAE involvement is a stronger efficacy signal than single-organ irAE, but this benefit is setting-dependent.
- Organ systems do not co-occur randomly; The co-occurrence rate of certain pairs (e.g. dermatologic–endocrine) are decreased, suggesting distinct biological pathways.
- Organ-specific survival associations vary by treatment line, which may guide personalized monitoring and risk-benefit assessment.

CONCLUSION

- Spatial co-occurrence patterns of irAEs provide additional **prognostic information** beyond single-organ events.
- The non-random co-occurrence and setting-specific organ distribution may help **clarify the mechanistic** link between irAE patterns and anti-PD-(L)1 efficacy in NSCLC.
- These findings support integrated **irAE phenotyping** in future immunotherapy trials and clinical practice.



Thank You.●