RESIDENT AND MEDICAL STUDENT SECTION

SIO RMSS Research Digest - April 2025

The Society of Interventional Oncology (SIO) 2025 Annual Scientific Meeting featured a wonderful session entitled “Must-Know Papers”, which featured six landmark manuscripts within the field of interventional oncology.

In this inaugural research digest brought to you by the SIO Resident and Medical Student Section (RMSS), we summarize and discuss each of these six landmark papers, in order to help readers unpack these studies and integrate important findings/takeaways into their practice.

This research digest is brought to you by research digest authors and RMSS research subcommittee members Sara Abosabie (MD/PhD Candidate), Madelon Dijkstra MD/PhD, and Dogan Polat MD; by digest editor and RMSS resident co-chair Gabriel Knight MD; and by digest editor and RMSS faculty advisor Erica Alexander MD.

Paper #1: Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma (Finn et al.) (https://www.nejm.org/doi/full/10.1056/NEJMoa1915745)

Author: Sara Abosabie
Editors: Gabriel Knight and Erica Alexander

SUMMARY (METHODS, RESULTS):

This study, known as the IMbrave150 trial, was a global, open-label, phase 3 study evaluating first-line treatment in patients with unresectable hepatocellular carcinoma who had not received prior systemic therapy. 501 patients were randomized in a 2:1 ratio to receive either the combination of atezolizumab plus bevacizumab (336 patients) or sorafenib (165 patients) until unacceptable toxic effects or loss of clinical benefit occurred.

Co-primary End Points:

- Overall survival (OS) and progression-free survival (PFS) in the intention-to-treat population, assessed per RECIST 1.1

Key Findings:

- **Overall Survival:**
  - *Atezolizumab–Bevacizumab:* 12-month OS rate of 67.2% (95% CI, 61.3 to 73.1)
  - *Sorafenib:* 12-month OS rate of 54.6% (95% CI, 45.2 to 64.0)
  - Hazard ratio for death was 0.58 (95% CI, 0.42 to 0.79; P<0.001)
- **Progression-Free Survival:**
  - *Atezolizumab–Bevacizumab:* Median PFS of 6.8 months (95% CI, 5.7 to 8.3)
  - *Sorafenib:* Median PFS of 4.3 months (95% CI, 4.0 to 5.6)
  - Hazard ratio for disease progression or death was 0.59 (95% CI, 0.47 to 0.76; P<0.001)
- **Safety Profile:**
  - Grade 3 or 4 adverse events occurred in 56.5% of patients receiving atezolizumab–bevacizumab versus 55.1% with sorafenib
  - Grade 3 or 4 hypertension was noted in 15.2% of the atezolizumab–bevacizumab group, while other high-grade toxic effects were infrequent

IMPORTANT TAKEAWAYS/DISCUSSION:

- Atezolizumab plus bevacizumab significantly improved overall survival and progression-free survival compared to sorafenib, demonstrating a 42% reduction in the risk of death.
- The combination therapy extended median PFS by approximately 2.5 months and yielded higher 12-month survival rates relative to sorafenib.
- The safety profiles were comparable between the two treatment groups, with adverse events that were manageable and consistent with known profiles for each agent.
- These findings underscore the clinical benefit of targeting both the PD-L1 and VEGF pathways in unresectable hepatocellular carcinoma and support the adoption of atezolizumab plus bevacizumab as a new standard of care in this patient population.

KEY FIGURES:

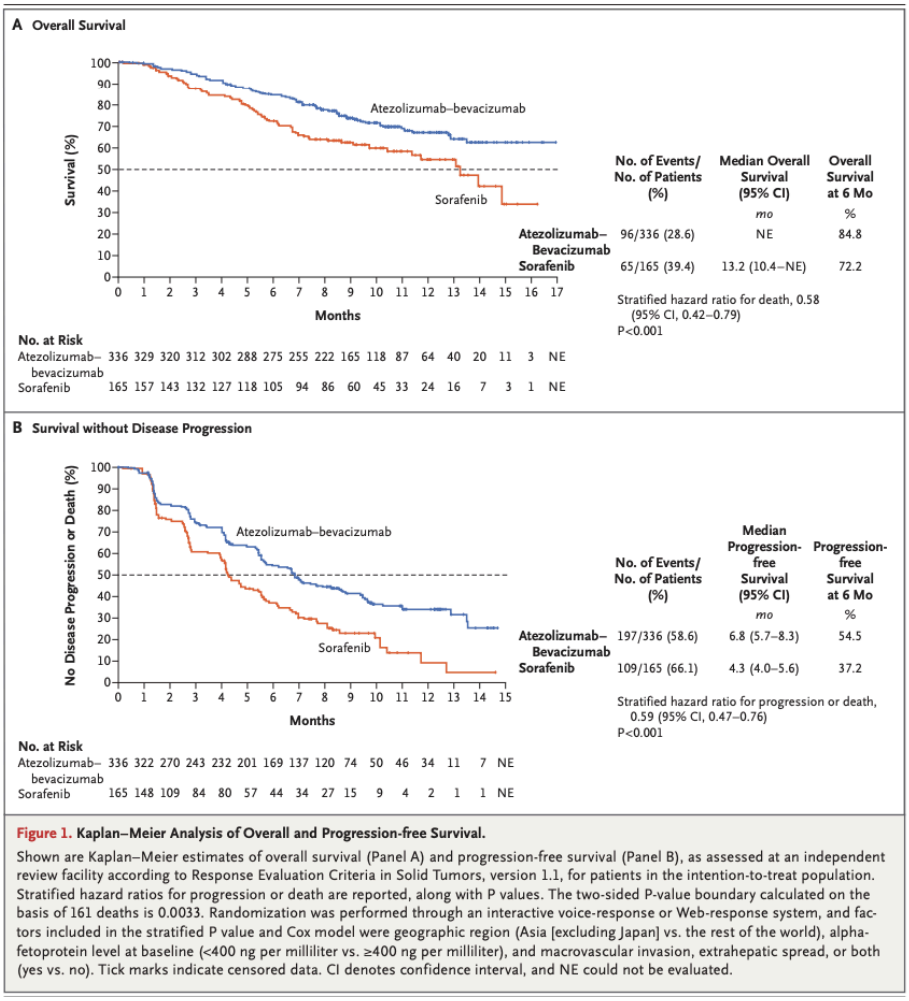


Figure 1. Kaplan–Meier Analysis of Overall and Progression-free Survival.

Shown are Kaplan–Meier estimates of overall survival (Panel A) and progression-free survival (Panel B), as assessed at an independent review facility according to Response Evaluation Criteria in Solid Tumors, version 1.1, for patients in the intention-to-treat population. Stratified hazard ratios for progression or death are reported, along with P values. The two-sided P-value boundary calculated on the basis of 161 deaths is 0.0033. Randomization was performed through an interactive voice-response or Web-response system, and factors included in the stratified P value and Cox model were geographic region (Asia [excluding Japan] vs. the rest of the world), alpha-fetoprotein level at baseline (<400 ng per milliliter vs. ≥400 ng per milliliter), and macrovascular invasion, extrahepatic spread, or both (yes vs. no). Tick marks indicate censored data. CI denotes confidence interval, and NE could not be evaluated.

Paper #2: Tremelimumab plus Durvalumab in Unresectable Hepatocellular Carcinoma (Abou-Alfa et al.)
(https://evidence.nejm.org/doi/full/10.1056/EVIDoa2100070)
Author: Sara Abosabie
Editors: Gabriel Knight and Erica Alexander

SUMMARY (METHODS, RESULTS):
The HIMALAYA trial was a global, open-label, phase 3 study evaluating first-line treatment in patients with unresectable hepatocellular carcinoma who had not received prior systemic therapy. 1171 patients were randomized into three arms:

- **STRIDE Regimen (393 patients):** A single high priming dose of tremelimumab (300 mg) followed by durvalumab (1500 mg every 4 weeks)
- **Durvalumab Monotherapy (389 patients):** 1500 mg every 4 weeks
- **Sorafenib (389 patients):** 400 mg twice daily

Primary Endpoint:

- Overall survival (OS) from randomization

Secondary efficacy Endpoints:

- Progression-free survival
- Time to progression
- Objective response rate
- Patient-reported outcomes (quality of life)
- Safety (including treatment-emergent adverse events and immunogenicity)

Key Findings:

- **Overall Survival:**
  - *STRIDE:* Median OS of 16.43 months
  - *Sorafenib:* Median OS of 13.77 months
  - Hazard ratio (HR) for STRIDE vs. sorafenib was 0.78 (96.02% CI, 0.65 to 0.93; *P* = 0.0035)
  - *Durvalumab:* Median OS of 16.56 months, demonstrating noninferiority to sorafenib (HR = 0.86; noninferiority margin <1.08)
- **Long-Term Survival Rates:**
  - At 36 months: 30.7% (STRIDE), 24.7% (durvalumab), and 20.2% (sorafenib)
- **Progression-Free Survival:**

    - No significant differences were observed among the three arms
- **Response Rates:**
    - Confirmed objective response rates were 20.1% with STRIDE, 17.0% with durvalumab, and 5.1% with sorafenib
- **Safety Profile:**
    - Grade 3/4 treatment-emergent adverse events were reported in 50.5% (STRIDE), 37.1% (durvalumab), and 52.4% (sorafenib) of patients

IMPORTANT TAKEAWAYS/DISCUSSION:

- Durvalumab monotherapy was noninferior to sorafenib, supporting its viability as a treatment option.
- The STRIDE regimen significantly improved overall survival compared to sorafenib, suggesting that the addition of a single high priming dose of tremelimumab enhances the clinical benefit of durvalumab in unresectable hepatocellular carcinoma.
- Although progression-free survival was similar across groups, the higher response rates and longer duration of response with STRIDE, as well as increased overall survival, indicate potential long-term benefits.
- The safety profiles were consistent with known effects of these agents, with manageable adverse events across the treatment arms.
- Like the IMbrave150 trial described above, the results of the present study support further investigation into immunotherapy combinations and may help refine patient selection and treatment strategies in hepatocellular carcinoma.

KEY FIGURES:

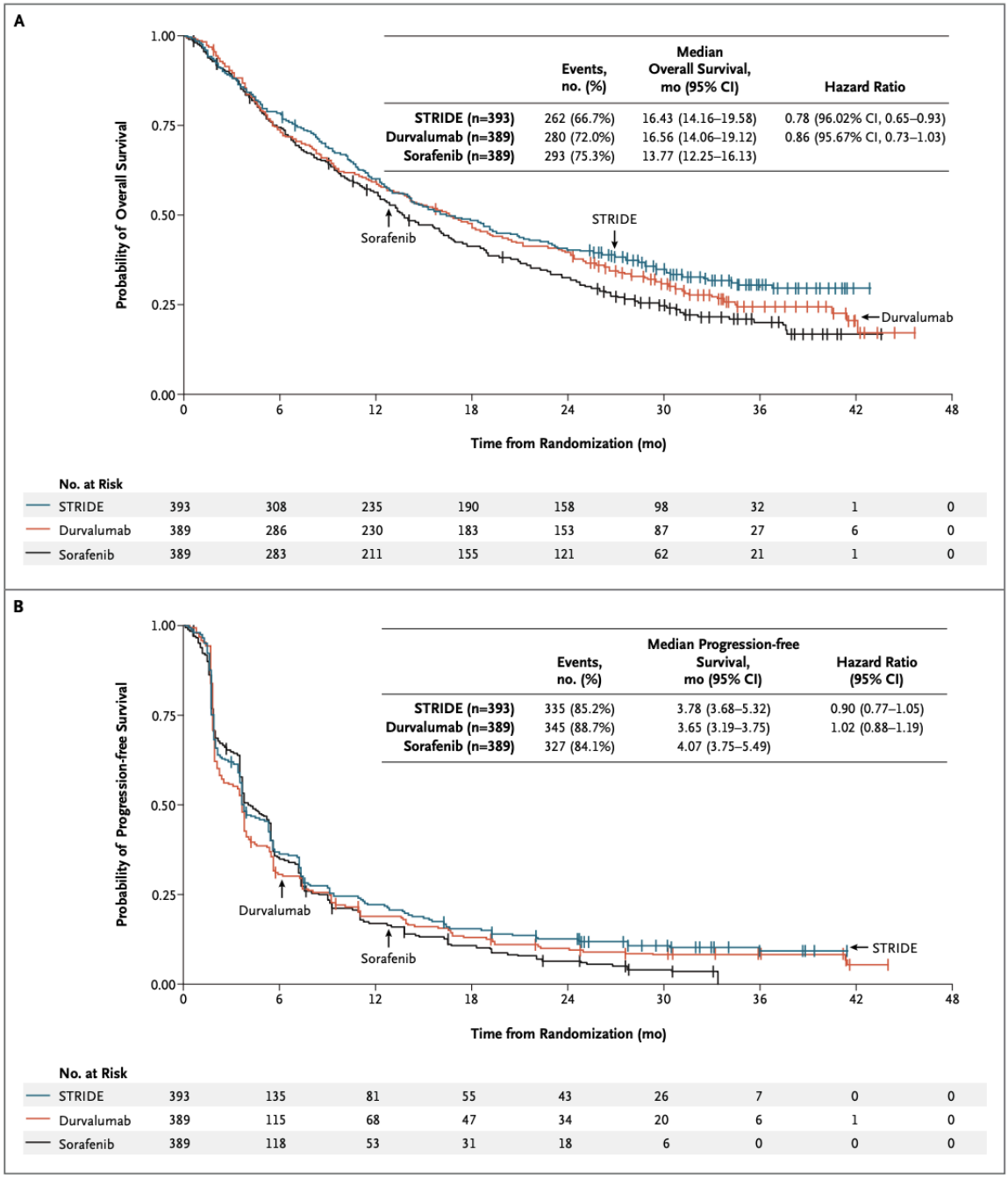


Figure 1. Kaplan–Meier Estimates of Overall Survival and Progression-Free Survival in the Intent-to-Treat Population.

Kaplan–Meier curves of overall survival (Panel A) and progression-free survival (Panel B) in the intent-to-treat population. Stratified hazard ratios for death are reported. Tick marks indicate censored data. CI denotes confidence interval and STRIDE Single Tremelimumab Regular Interval Durvalumab.

Paper #3: Intraprocedural Versus Initial Follow-up Minimal Ablative Margin Assessment After Colorectal Liver Metastasis Thermal Ablation: Which One Better Predicts Local Outcomes? (Lin et al.)
(https://pubmed.ncbi.nlm.nih.gov/37812469/)
Author: Dogan Polat
Editors: Gabriel Knight and Erica Alexander

SUMMARY (METHODS, RESULTS):

This retrospective, single-institution study evaluated the prognostic value of minimal ablative margin (MAM) assessment using intraprocedural vs. initial follow-up CT in predicting local tumor progression (LTP) after microwave and radiofrequency ablation for colorectal liver metastases (CLM). In brief, sufficient ablative margin is considered as a critical factor for local tumor control. The study analyzed 133 ablated tumors in 68 patients, excluding cases with residual tumors or insufficient follow-up.

- Primary Outcome: 1-year local tumor progression (LTP).
- Key Findings:
    - LTP Rate: 17% (22/133 tumors) over a median follow-up of 30.3 months.
    - Median MAM: 4.7 mm on intraprocedural CT vs. 0 mm on initial follow-up CT ($p < 0.001$).
    - Ablation Zone Volume: 27 mL (intraprocedural) vs. 16 mL (follow-up) ($p < 0.001$).
    - Predictive Accuracy (AUC for 1-year LTP):
        - Intraprocedural MAM: 0.89 (95% CI, 0.83–0.94).
        - Follow-up MAM: 0.66 (95% CI, 0.54–0.76) ($p < 0.001$).
    - Independent LTP Predictor: 0 mm MAM on intraprocedural CT (HR 11.9, $p < 0.001$).

IMPORTANT TAKEAWAYS/DISCUSSION:

- Intraprocedural CT-based MAM assessment significantly outperformed initial follow-up CT in predicting LTP and should :
    - It provides real-time, actionable feedback, allowing immediate treatment modifications.
    - Follow-up MAM is less reliable due to ablation zone involution and imaging variability.
- A 5-mm MAM threshold on intraprocedural CT remains the standard:
    - LTP risk is significantly higher when MAM < 5 mm.
    - No LTP was observed when MAM > 3.2 mm on intraprocedural CT.
- Limitations of Initial Follow-up CT for MAM Assessment:

    - Significant shrinkage (~38%) of the ablation zone over time reduces accuracy.
    - Highly variable ablation zone involution makes standardization challenging.
- Clinical Implications:
    - Assessing ablation margins real-time/intra-procedurally is more predictive of local tumor control than via post-procedural follow-up CT. Real-time assessment of ablative margins during the procedure should be the preferred method for determining the success of ablation therapy.
    - Post-ablation adjustments (e.g., additional ablation when MAM < 5 mm) could reduce LTP rates.

KEY FIGURES:

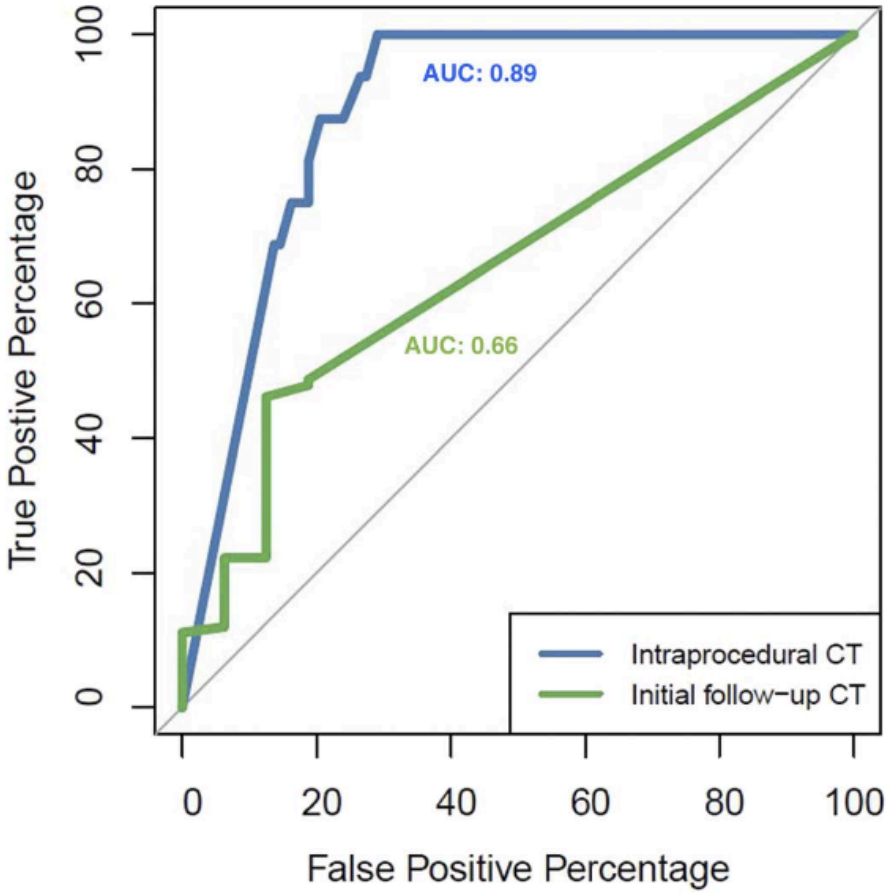


FIGURE 4. Receiver operating characteristic curves for predicting 1-year local tumor progression by minimal ablative margin quantified by intraprocedural versus initial follow-up CT images.

TABLE 2. Ablation Assessment by Intraprocedural and Initial Follow-up Postablation Contrast-Enhanced CT Images

Variables	Intraprocedural CT	Initial Follow-up CT	*P*
Volume of ablation zone, mL	27 (17, 52)	16 (9, 37)	<0.001
Minimal ablative margin, mm	4.7 (1.5, 6.0)	0 (0, 2.3)	<0.001
Minimal ablative margin			<0.001
0	27 (20%)	73 (55%)	
>0 to <5 mm	41 (31%)	45 (34%)	
≥5 to <10 mm	61 (46%)	14 (10%)	
≥10 mm	4 (3%)	1 (1%)	
Volume of tissue at risk for progression, mL	0.01 (0, 0.5)	0.9 (0.3, 1.9)	<0.001

Data are numbers of tumors with percentages or median with interquartile range.

Paper #4: MRI-guided stereotactic ablative body radiotherapy versus CT-guided percutaneous irreversible electroporation for locally advanced pancreatic cancer (CROSSFIRE): a single-centre, open-label, randomised phase 2 trial (Timmer et al.) (https://pubmed.ncbi.nlm.nih.gov/38513683/)

Author: Dogan Polat
Editors: Gabriel Knight and Erica Alexander

SUMMARY (METHODS, RESULTS):

The CROSSFIRE trial was a randomized phase 2 superiority study comparing MRI-guided stereotactic ablative body radiotherapy (SABR) and CT-guided irreversible electroporation (IRE) in locally advanced pancreatic cancer (LAPC) after FOLFIRINOX chemotherapy. 68 patients were randomized 1:1 to receive either SABR (5 fractions of 8 Gy) (34 patients) or IRE (34 patients) under CT guidance.

- Primary Endpoint: Overall survival (OS) from randomization
- Secondary Endpoints: Progression-free survival (PFS), treatment safety, quality of life, and immune response analysis.
- Key Findings:
    - Median OS: 16.1 months (SABR) vs. 12.5 months (IRE) (HR 1.39, p=0.21).
    - Progression-Free Survival: No significant difference (HR 0.82, p=0.48) between SABR and IRE.
    - Adverse Events: 63% (SABR) vs. 59% (IRE); Grade 3–5: 16% (SABR) vs. 25% (IRE).
    - Distant PFS: Longer in IRE (13.2 vs. 8.5 months, p=0.007).
    - Quality of Life: Stable up to 6 months, then declined due to disease progression.
    - Immune Response: Both treatments induced transient immune activation; IRE showed PD-1 upregulation.

The trial was halted early for futility (conditional probability of superiority = 0.13).

IMPORTANT TAKEAWAYS/DISCUSSION:

- While both SABR and IRE offer local disease control, neither demonstrated superiority/survival benefit, emphasizing careful patient selection and further study of their role in multimodal treatment, and reinforcing need for further trials.
- IRE had a higher rate of treatment-related grade 3–5 adverse events (22% vs. 6%).
- Both treatments suggest a potential immunomodulatory effect.

- IRE's immune effects support investigation of combination strategies with immunotherapy.
    - Stay tuned for future SIO research digests for discussions of locoregional therapy + immunotherapy (LRT + IO)!
- One limitation of this trial was that it stopped early for futility, preventing definitive conclusions on marginal differences in survival.
- Future research should compare these approaches with systemic therapy alone (e.g., forthcoming LAPSTAR trial).

KEY FIGURES:

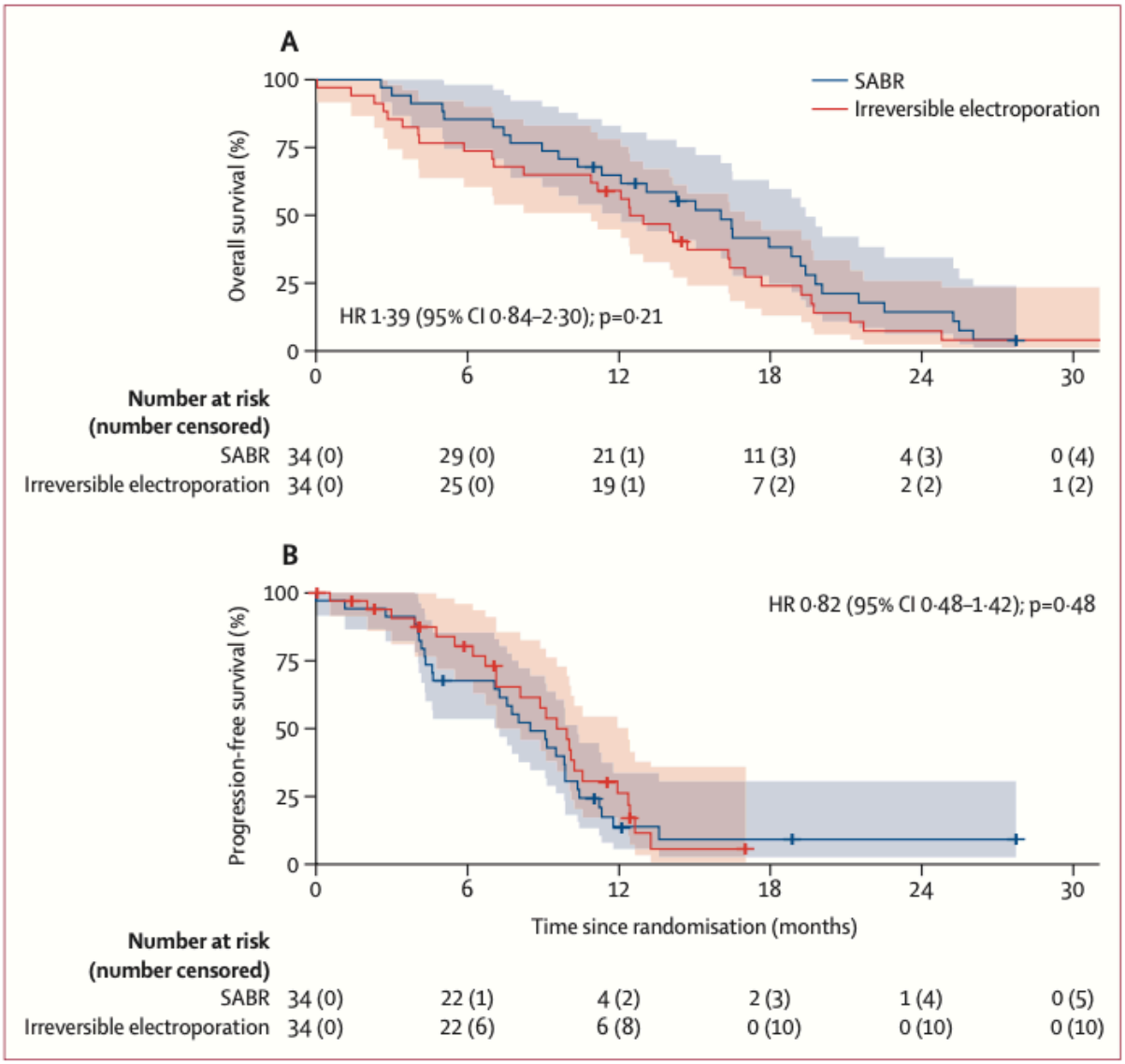


Figure 2: **Kaplan-Meier curves for overall survival (A) and progression-free survival (B)**
SABR=stereotactic ablative body radiotherapy. HR=hazard ratio.

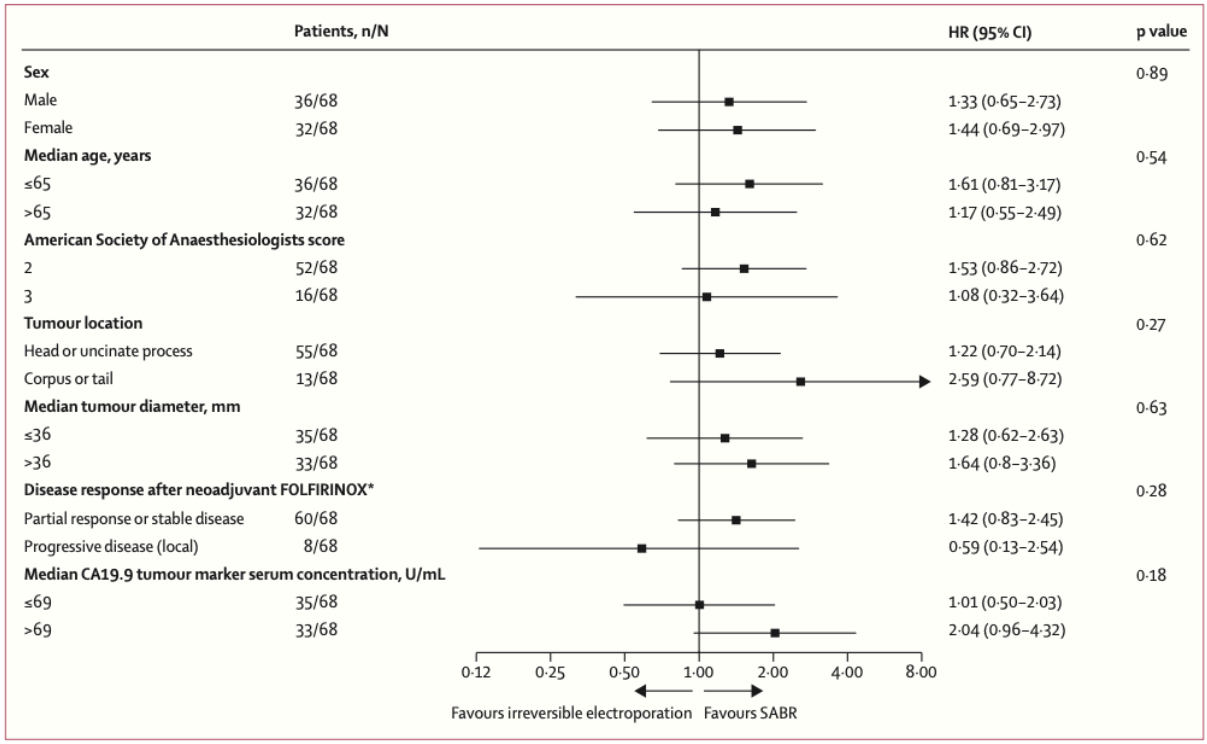


Figure 4: **Subgroup analysis of overall survival**

HRs higher than 1 favour SABR and HRs below 1 favour irreversible electroporation. HR=hazard ratio. SABR=stereotactic ablative body radiotherapy. RECIST=Response Evaluation Criteria in Solid Tumours. *As per RECIST (version 1.1) criteria.

Paper #5: Sublobar Resection, Stereotactic Body Radiation Therapy, and Percutaneous Ablation Provide Comparable Outcomes for Lung Metastasis-Directed Therapy (Gits et al.)
(https://pubmed.ncbi.nlm.nih.gov/38103730/)
Author: Madelon Dijkstra
Editors: Gabriel Knight and Erica Alexander

SUMMARY (METHODS, RESULTS):

The multihospital retrospective review and propensity matched analysis focused on comparing outcomes of three different metastasis-directed therapies (MDT) for lung metastases: sublobar resection (SLR), stereotactic body radiation therapy (SBRT), and percutaneous ablation (PA). A total of 644 lung MDT courses were delivered to 511 patients between January 2015 and December 2020 at a single cancer center. The breakdown of these treatments was 243 courses of SLR, 274 courses of SBRT, and 127 courses of PA, with a median follow-up of 22 months.

Key outcomes collected for analysis included overall survival (OS), local progression (LP), and toxicity outcomes. The study used multivariable models and propensity-weighted analysis to adjust for potential confounders.

The main findings include:

- Overall Survival (OS):
  - SLR: 2-year OS was 80.3%
  - SBRT: 2-year OS was 83.8%
  - PA: 2-year OS was 4.1%
- Local Progression (LP):
  - SLR: 2-year LP was 63.3%
  - SBRT: 2-year LP was 9.6%
  - PA: 2-year LP was 11.7%
- Lesion Size Impact:
  - Larger lesion size (per 1 cm increase) was associated with worse overall survival (HR = 1.24; P = .003) and greater risk of local progression (HR = 1.50; P < .001).
- Local Progression Risk Comparison:
  - There was no significant difference in local progression risk between SLR and PA.
  - SBRT was associated with a decreased risk of local progression compared to SLR (HR = 0.26; P = .023).

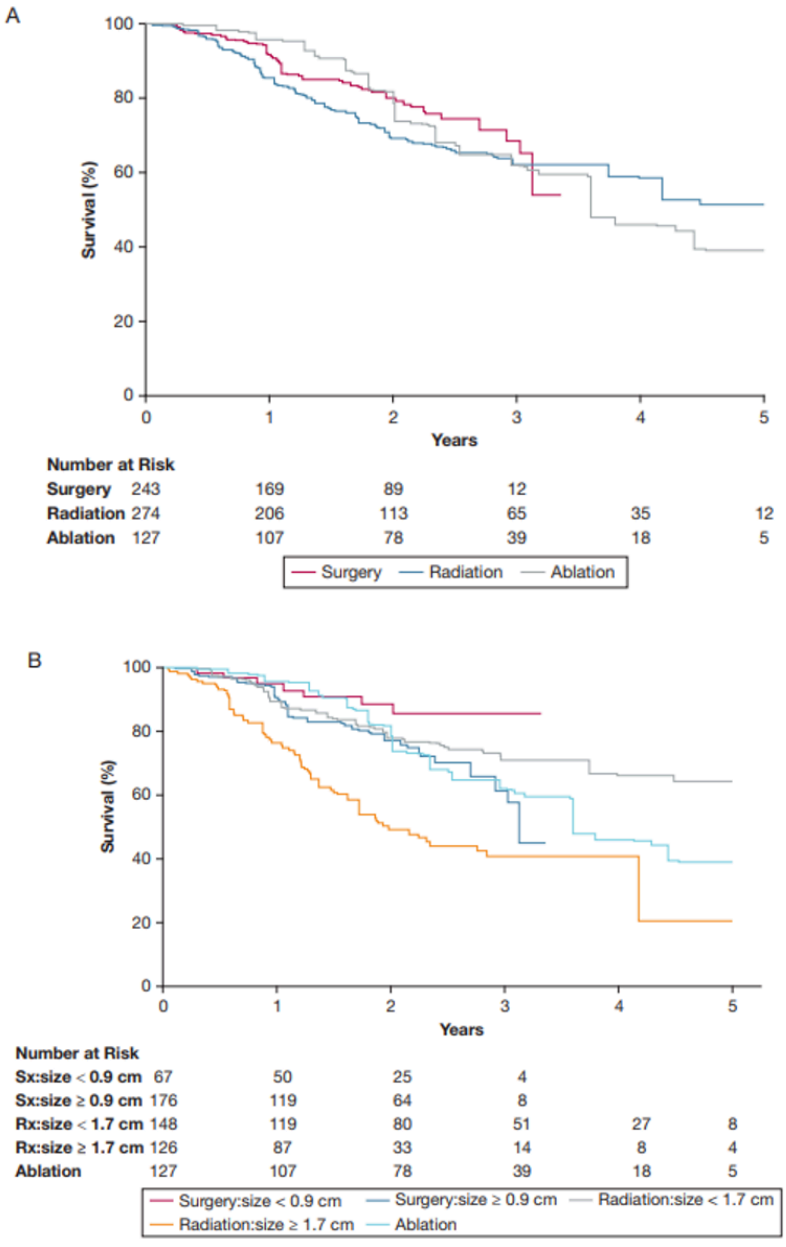
- Toxicity:
    - Rates of severe toxicity were low across all three modalities (ranging from 2.1% to 2.6%) and were not significantly different among the treatment groups.

IMPORTANT TAKEAWAYS/DISCUSSION:

- No Significant Difference in Overall Survival between SLR, SBRT, and PA
- Local Control and Local Progression
    - SBRT was associated with a decreased risk of LP (HR, 0.26; 95% CI, 0.08-0.83; P = 0.023)
    - This suggests that SBRT may offer superior local control, particularly in preventing tumor recurrence at the treatment site.
        - As the authors discuss, this difference could also relate to challenges in defining LP in the SBRT cohort, because of the presence of radiation-associated changes in lung parenchyma, which underscores the importance of prolonged follow-up.
- Impact of Lesion Size
    - Larger tumors are associated with worse survival and local progression outcomes, which aligns with previous research that emphasizes the importance of early detection and treatment for smaller metastases.
- Low Toxicity
    - The low incidence of severe toxicity (2.1%-2.6%) across all modalities supports the safety of these treatments.
    - This is particularly important for patient quality of life, as these treatments are not associated with substantial adverse effects.
- Importance of a Multidisciplinary Approach
    - Given the comparable overall survival and the effectiveness of all three treatments, the study emphasizes the importance of a multidisciplinary approach to treatment planning.
    - Selecting the most appropriate lung MDT modality often includes decisions regarding the likelihood of a patient tolerating invasive intervention, lesion location, and lung parenchymal sparing.
        - SBRT is a preferred option for patients with high surgical risk or centrally located tumors.
        - PA may be favored for lung parenchymal preservation in patients with multiple prior treatments.
- Further Research Needed
    - Limited by retrospective design.
    - Further prospective, randomized controlled trials are needed to more definitively compare these treatment modalities and establish more specific guidelines for patient management.
- Conclusions:

- Among 644 patients treated with SLR, SBRT, and PA for lung metastases, all modalities had equivalent outcomes for OS, with low risk of severe toxicity with each modality. Given excellent local control across MDT options, a multidisciplinary approach is beneficial for patient triage and longitudinal management.

KEY FIGURES:



KM estimated overall survival curves adjusted for inverse probability treatment weights and separated by (A) treatment modality and (B) treatment modality and optimal lesion size cutpoint.

Paper #6: Percutaneous Microwave Ablation Versus Robot-Assisted Partial Nephrectomy for Stage I Renal Cell Carcinoma: A Propensity-Matched Cohort Study Focusing Upon Long-Term Follow-Up of Oncologic Outcomes (Chlorogiannis et al.) (https://pubmed.ncbi.nlm.nih.gov/38561521/)

Author: Madelon Dijkstra
Editors: Gabriel Knight and Erica Alexander

SUMMARY (METHODS, RESULTS):

This retrospective study aimed to compare the long-term oncologic outcomes of percutaneous computed tomography-guided microwave ablation (MWA) and robot-assisted partial nephrectomy (RAPN) in patients with stage I (T1a and T1b) renal cell carcinoma (RCC).

The study included 142 patients who underwent either MWA or RAPN between 2012 and 2022. After applying propensity score matching to adjust for baseline differences, 71 patients in each group were analyzed. The mean age was 70 ± 10 years for the MWA group and 60 ± 9 years for the RAPN group. 129 T1a tumors were analyzed compared to 29 T1b tumors.

At an 8-year follow-up, the estimated survival rates were as follows:

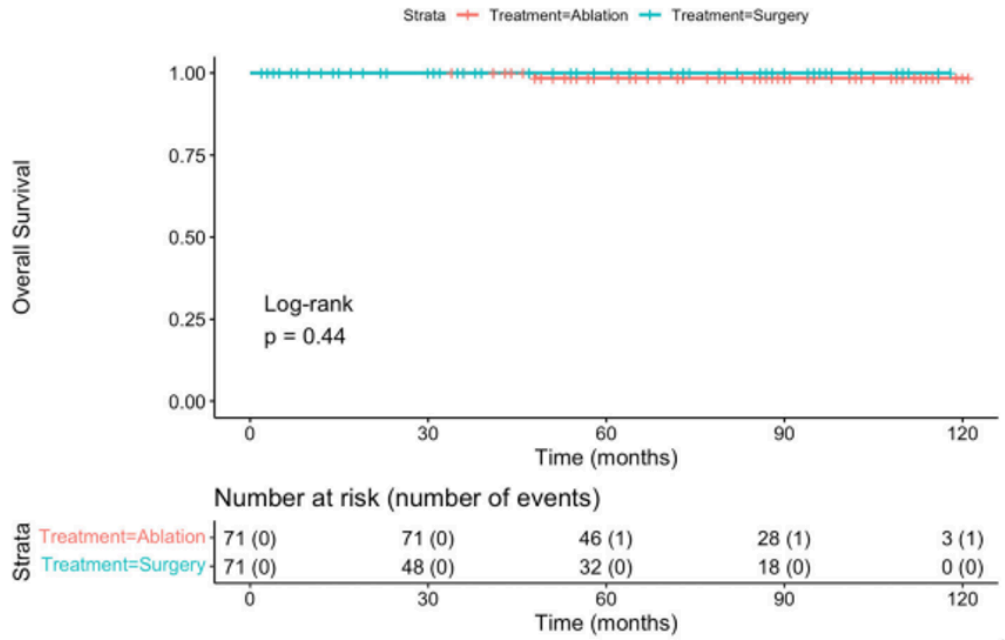
- MWA Group:
  - Overall Survival: 98% (95% CI 95–100%)
  - Recurrence-Free Survival: 97% (95% CI 93–100%)
  - Metastasis-Free Survival: 97% (95% CI 93–100%)
- RAPN Group:
  - Overall Survival: 100% (95% CI 100–100%)
  - Recurrence-Free Survival: 98% (95% CI 94–100%)
  - Metastasis-Free Survival: 98% (95% CI 94–100%)
- MWA vs. RAPN
  - Statistical analysis using the log-rank test revealed no significant differences between the two groups in overall survival ($p = 0.44$), recurrence-free survival ($p = 0.67$), or metastasis-free survival ($p = 0.67$).

CIRSE Grade I complications were observed in 5 patients (4 small perinephric hematomas and 1 small urinoma), all of whom were in the MWA group, without the need for further treatment.

IMPORTANT TAKEAWAYS/DISCUSSION:

- Comparable Oncologic Outcomes between MWA and RAPN
    - The study found that both MWA and RAPN offer similar long-term oncologic outcomes for patients with stage I RCC. This suggests that MWA could be a viable alternative to RAPN, especially for patients who may not be candidates for surgery.
- Safety Profiles:
    - While the study primarily focused on oncologic outcomes, the safety profiles of MWA and RAPN are also important considerations.
    - Previous studies have indicated that MWA is associated with shorter hospital stays and lower complication rates compared to RAPN.
    - In the present study, while all complications occurred in the MWA group, all complications were CIRSE grade 1 (i.e. not requiring treatment), and the overall rate of these minor complications was relatively low.
- Importance of Patient Selection:
    - Given the comparable survival rates, treatment decisions should consider patient-specific factors, including comorbidities, tumor characteristics, and patient preferences.
    - A multidisciplinary approach is essential to determine the most appropriate treatment modality.
- Limitations:
    - As a retrospective study, the findings are subject to inherent biases.
    - Prospective randomized controlled trials are needed to confirm these results and provide more definitive guidance on treatment selection.
    - While there was no difference in the oncologic outcomes in the subgroup of patients with T1b tumors, the relatively small sample size does not allow for safe conclusions to be drawn; nonetheless, it still represents real-world data.
- Conclusions
    - Both MWA and RAPN are equally effective in terms of oncologic outcomes for T1a RCC, even at long-term follow-up.
        - These results were consistent for both T1a and T1b tumors, noting limitations for T1b tumors described above.
    - Individualized treatment planning, considering patient and tumor characteristics, is crucial for optimal management.

KEY FIGURES:



Kaplan–Meier log-rank test for recurrence-free survival curve comparing MWA (71 patients) and RAPN (71 patients).