

# Yttrium-90 Radioembolization and Concomitant Systemic Gemcitabine, Cisplatin, and Capecitabine as the First-Line Therapy for Locally Advanced Intrahepatic Cholangiocarcinoma

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## Background

- The MISPHEC (Yttrium-90 Microspheres in Cholangiocarcinoma) single-arm Phase 2 trial demonstrated the safety and efficacy of combining radioembolization (TARE) with gemcitabine and cisplatin (Gem/Cis) as the first-line treatment for unresectable intrahepatic cholangiocarcinoma (iCCA)
- Capecitabine has been shown effective as a radiosensitizer combined with TARE for primary and secondary liver tumors.
- This study aimed to evaluate the effectiveness of combined regimen using Gem/Cis/Cap/TARE quadruple therapy as a first-line treatment for locally advanced, biopsy-proven iCCAs that are initially unresectable or technically challenging to resect

## Methods and Results



- Glass Y90 microspheres (Therasphere, Boston Scientific, Marlborough, MA)
- Segmental artery using the medical internal radiation dose model with or without lobar dose using single compartment medical internal radiation dose model.
- All treatments were dosed with week-1 calibration delivered on Wednesday to Friday.
- From June 2018 to May 2022, 23 consecutive, biopsy-proven iCCA patients were enrolled; two patients did not tolerate neoadjuvant Gem/Cis; one patient was loss to follow-up.
- Multifocal Disease: 4/20 (20%). Central or Bilobar Disease: 18/20 (90%). Lymphadenopathy: 15/20 (75%) Median Tumor Size 6.1cm, IQR 4.4-8cm.
- Days between TARE and Gem/Cis: 87 days, IQR 65-96 days
- Two patients had two session; 18 patients had single session. Segmental: n=6; Lobar: n=3; Combined: n=11.
- Segmental deliveries n=22 (median 258Gy, IQR: 244-318Gy) Lobar deliveries n=14 (median 155.5Gy, 149-160Gy)

**20 patients**

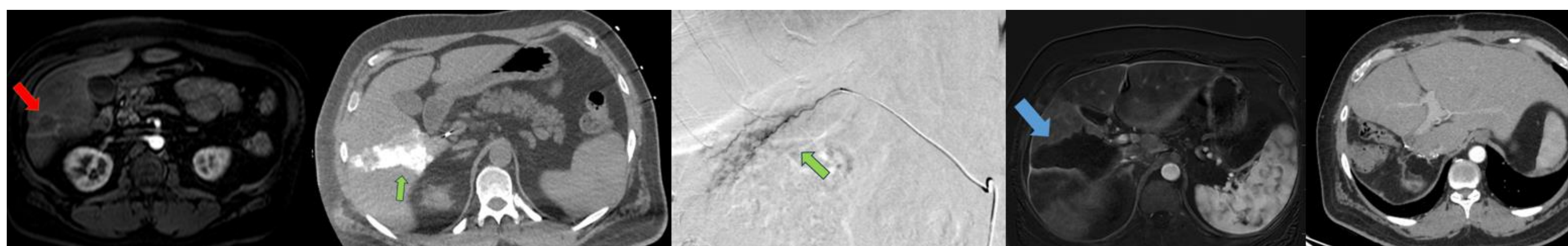
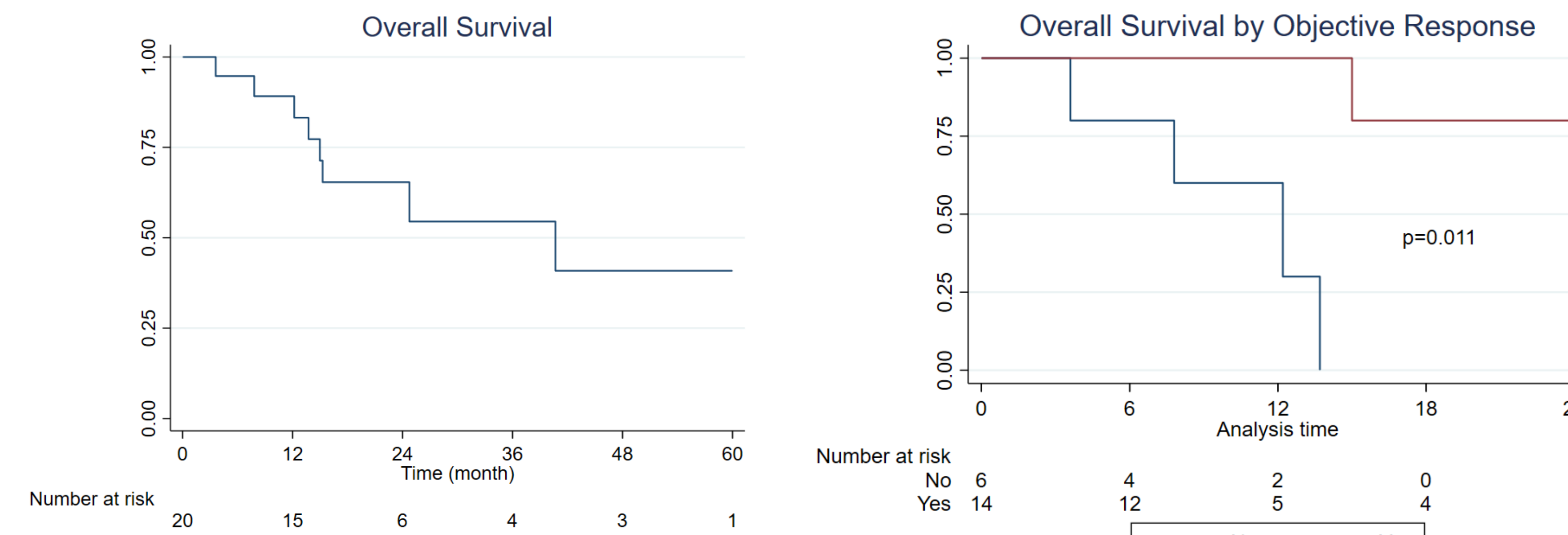
- mOS: 0.7 months (95%CI:15.0-not reached) mo
- 1 year survival: 89.2% (95%CI: 63.2-97.2%)
- 3-year survival: 54.5% (95%CI: 25.3-76.5%)

**Objective Response N=14 (70%)**

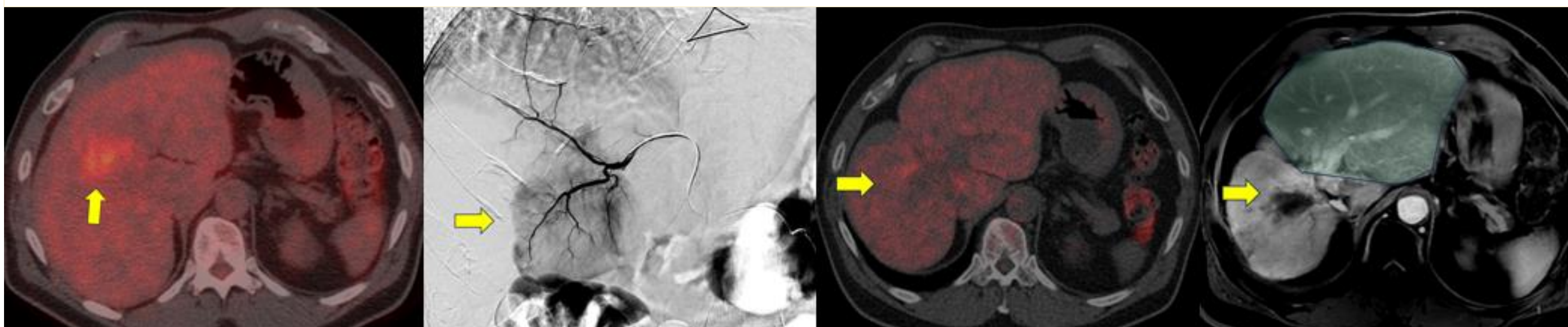
- Resection (n=9); LDLT Evaluation (n=3)
- Stable Disease (n=1); Palliative care given poor performance status
- Progressive Disease: FOLFOX 2<sup>nd</sup> Line (n=3); Erdafitinib 2<sup>nd</sup> Line (n=1)

**9 patients (45%) downstaged to surgery**

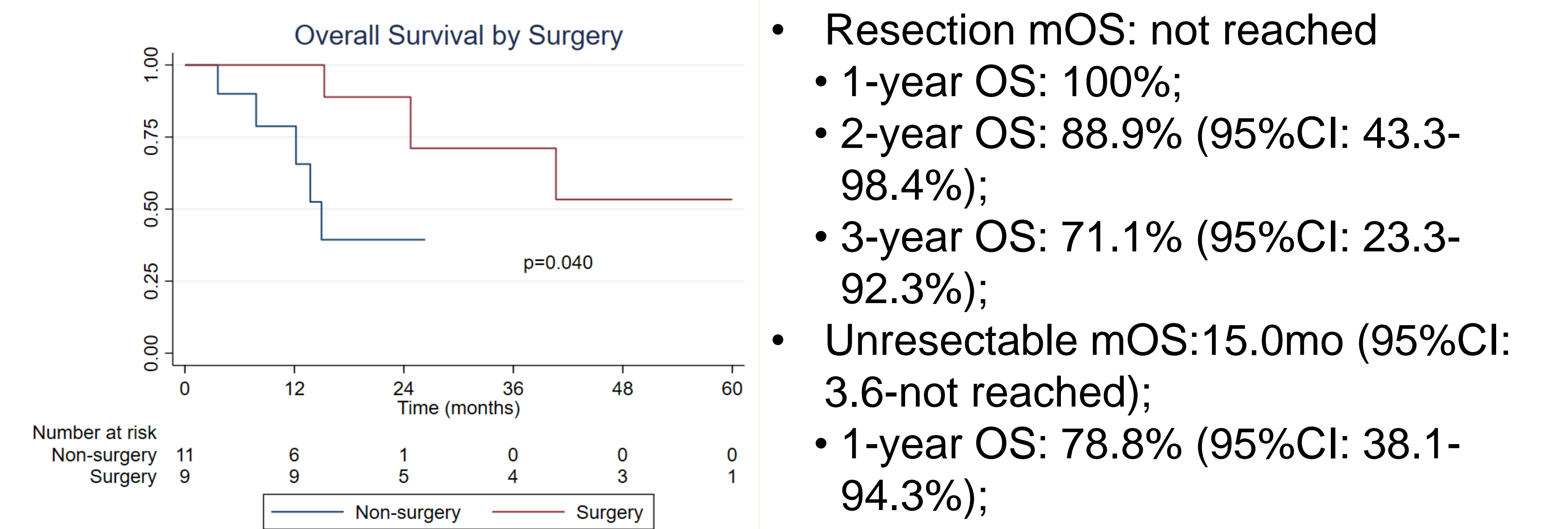
- R0 Resection: n=6, 66.7%
- > 90% Pathologic Necrosis: n=8, 88.9%



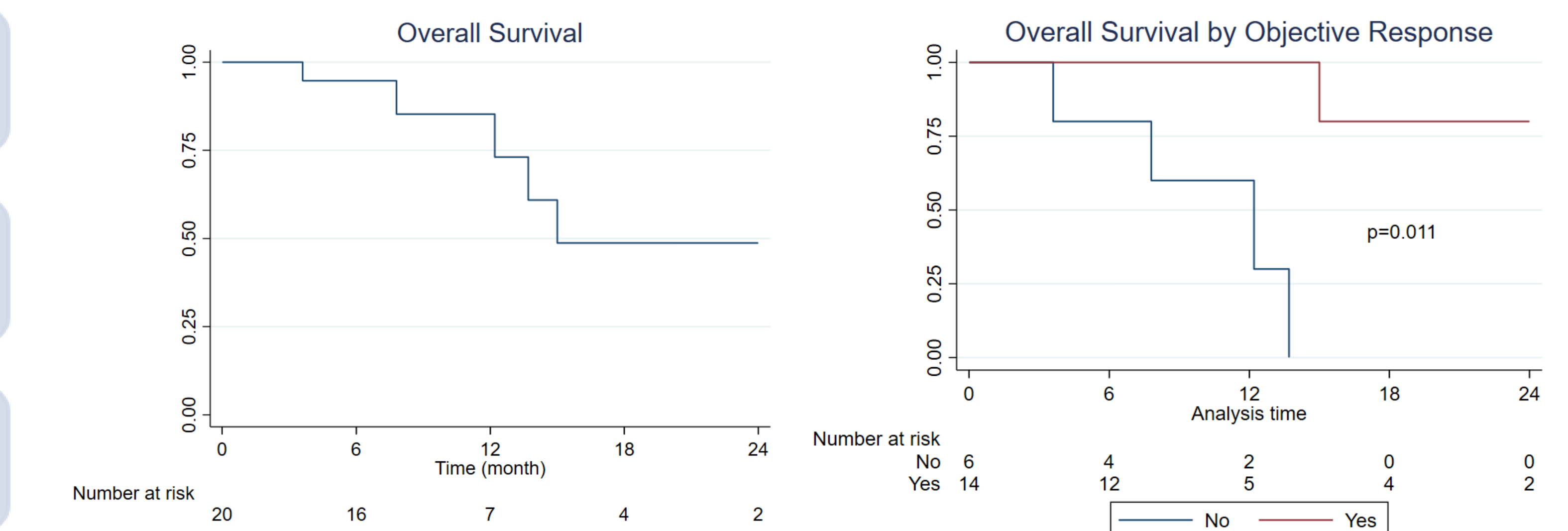
**Case 1:** Right sided tumor. A) Pre-treatment 4.0 cm enhancing tumor (red arrow) on magnetic resonance imaging (MRI). B) Intraprocedural computed tomography with C) catheter-directed arteriography shows vascular supply from segment 6/7 branch of right hepatic artery and tumor coverage (green arrows): 399Gy (segment6) + 409Gy (segment 6/7), 157Gy (right lobar). D) post-radioembolization MRI shows treatment effect (blue arrow) and lack of enhancement. E) Post right hepatectomy changes and left lobe hypertrophy.



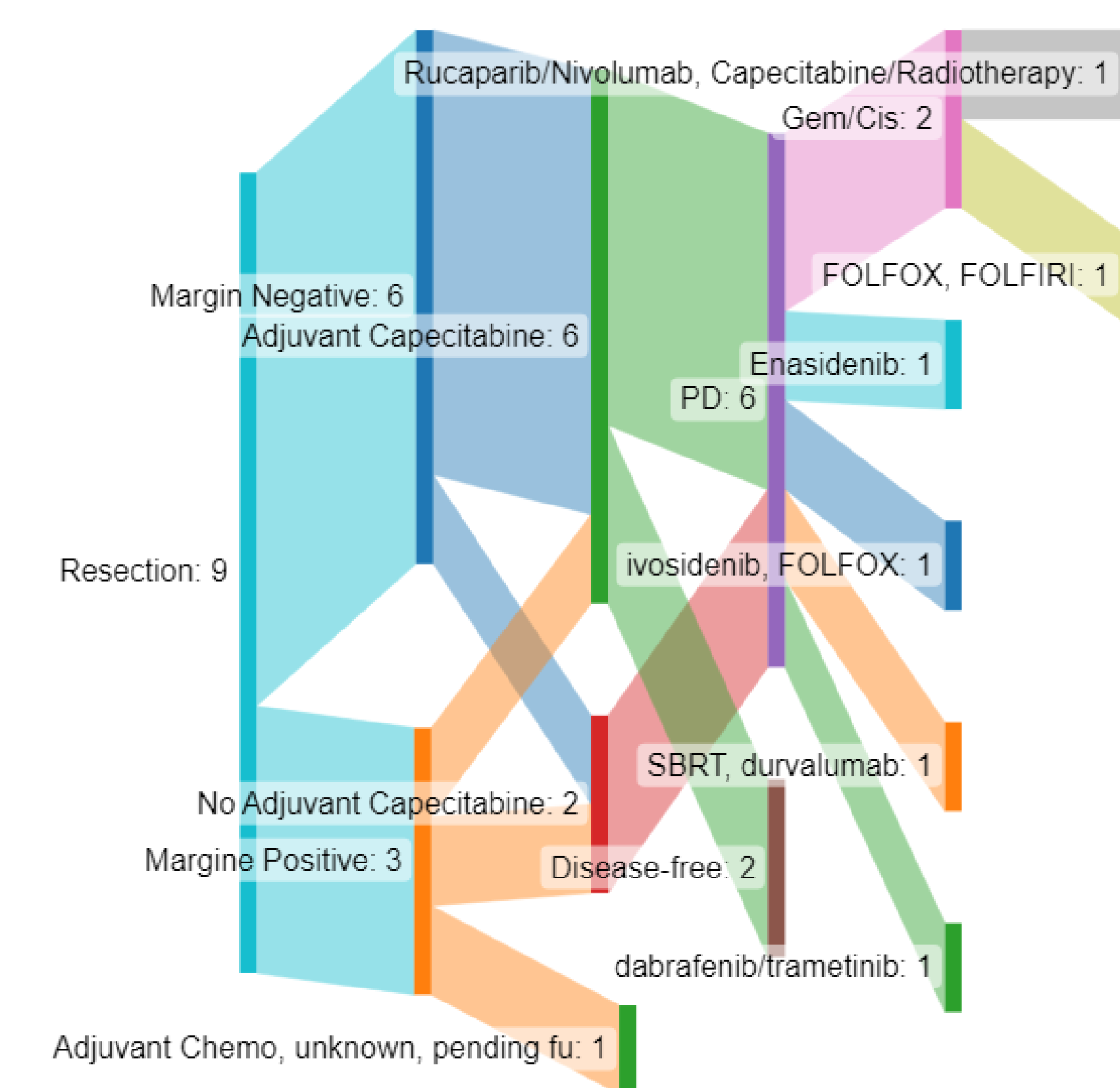
**Case 2:** Central hepatic iCCA treated with 423Gy segment 4 dose and 156Gy right lobar dose. FDG uptake decreased after treatment with left lobe hypertrophy



- Resection mOS: not reached
- 1-year OS: 100%;
- 2-year OS: 88.9% (95%CI: 43.3-98.4%);
- 3-year OS: 71.1% (95%CI: 23.3-92.3%);
- Unresectable mOS:15.0mo (95%CI: 3.6-not reached);
- 1-year OS: 78.8% (95%CI: 38.1-94.3%);
- 2-year OS: 39.4% (95%CI: 9.4-69.2%)



Overall Survival after censoring patients at surgery: mOS 15mo (95%CI:12.2-not reached); 1-year OS: 86.3% (95%CI: 50.5-96.3%); 2-year OS: 48.7% (95%CI: 15.6-75.7%). Objective Response confers improved survival rates: log-rank test p=0.011



- Adjuvant Therapy after Resection: 7/9 (77.8%)
- Not given in two patients due to non-compliance and prior side-effects
- Recurrent Disease after Resection: 6/9 (66.7%)
- Intrahepatic: n=2
- Extrahepatic: n=3
- Both: n=1
- No recurrence n=2, R0
- Pending Follow-up n=1, R1

## Conclusion

- TARE combined with Gem/Cis/Cap quadruple therapy was effective as a first-line therapy for locally advanced iCCA with an promising overall survival outcome.
- This combined first-line treatment regimen can downstage patients to curative surgery.
- Multidisciplinary approach with the implementation of TARE may offer benefit for downstaging tumors to resection and optimizing long-term survival.

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