Effect of Standardized Radiofrequency Ablation and Lyso-Thermosensitive Liposomal Doxorubicin (LTLD, ThermoDox®) on Overall Survival (OS) Among Patients with a Solitary 3-7cm Hepatocellular Carcinoma (HCC) Lesion: A HEAT Study Multivariate Analysis

Shi-Ming Lin (Chang Gung Memorial Hospital, Linkou, Taiwan), Won Young Tak (Kyungpook National University Hospital, Daegu, Korea), Hyunchul Rhim (Samsung University Hospital, Seoul, Korea), Yi-You Chiou (Taipei Veterans General Hospital, Taipei, Taiwan), Min Hua Chen (Beijing Cancer Hospital, Beijing, China), Soo Young Park (Kyungpook National University Hospital, Daegu, Korea), Jae Young Lee (Seoul National University Hospital, Seoul, Korea), Ja-Der Liang (National Taiwan University Hospital, Taipei, Taiwan), Riccardo Lencioni (University of Pisa School of Medicine, Pisa, Italy), Nicholas Borys (Celsion Corporation, Lawrenceville, NJ), Ronnie Poon (Queen Mary Hospital, Hong Kong, Hong Kong)

Purpose

The 701-patient HEAT Study compared RFA monotherapy versus RFA plus LTLD. No minimum RFA dwell time was required. Intent-to-treat analysis produced a negative finding, but subgroup analysis found a positive result among patients with a solitary lesion who received LTLD and ≥45 minutes RFA (standardized RFA, sRFA). The hazard ratio (HR) was 0.63 (95% CI: 0.39-1.01), a 37% OS risk reduction. We conducted a multivariate analysis to see if this positive result was due to other factors known to influence survival in HCC patients.

Patients and Methods

We estimated a Cox regression model among 446 patients with a solitary 3-7cm lesion. The model included study treatment (RFA alone versus RFA+LTLD), RFA dwell time (<45 minutes versus ≥45 minutes), study treatment/dwell time interaction term (RFA alone or RFA ≥45 minutes versus other), lesion diameter (3-5cm versus >5-7cm), Child-Pugh score (5, 6, or 7+), HCC etiology (any hepatitis B versus other), age (<65 versus ≥65), region (Taiwan/Korea, China/Hong Kong, or other), and RFA device (Covidien versus other).

Results

Taking eight prognostic and treatment factors into consideration, adding LTLD to sRFA had a favorable HR of 0.64 (95% CI: 0.40-1.03), a 36% OS risk reduction. Lesion diameter and Child-Pugh score were statistically significant prognostic factors in the solitary lesion subgroup while HCC etiology, age, region, and RFA device were not. Further survival follow-up through July 15, 2015 found an HR of 0.63 (95% CI: 0.43-0.93; p=0.02), a 37% OS risk reduction. Median OS was over two years longer (25.4 months) among the 138 sRFA + LTLD patients (median 79.0 months) than among the 147 sRFA monotherapy patients (median 53.6 months).

Conclusion

The positive effect of the sRFA and LTLD combination on survival cannot be attributed to known HCC prognostic factors. The 550-patient OPTIMA Study is now underway to confirm this effect.

Authorship

Shi-Ming Lin, MD
Won Young Tak, MD
Hyunchul Rhim, MD
Yi-You Chiou, MD
M.H. Chen, MDg
Soo Young Park, MD
Jae Young Lee, MD
Ja-Der Liang, MD
Riccardo Lencioni, MD
Nicholas Borys, MD
Ronnie Poon, MD