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PUBLICATION SUMMARY – LUNG

Multicenter Study of Metastatic Lung Tumors Targeted by Interventional Cryoablation Evaluation (SOLSTICE)

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OVERVIEW

- Multi-Center, prospective, single arm, phase II study
- 10 centers: 2 in EU and 8 in US
- N= 128 patients, 167 procedures, 224 lung metastases treated with cryoablation
- Patient follow-up at 12 and 24 months
- Treatment of 1-6 metastases for extrapulmonary cancers with max diameter of 3.5cm
- Primary efficacy objective was local recurrence-free survival of treated tumors
- Time to progression, metastatic disease and overall survival rates were estimated using Kaplan-Meier method
- Complications were monitored for 30 days post procedure
- Hospital stay varied: US median of 1 day (range 0-13 days) and Europe median of 3 days (range 0-7 days)

Surgical resection is the standard for treatment of patients with limited pulmonary metastatic disease, however many patients are not surgical candidates. Unfortunately, many patients will develop additional metastatic disease in the lung and repeat surgical treatment may not be an option due to technical concerns or limited pulmonary reserve. Cryoablative treatment of centrally located tumors, when technically feasible, may allow for combination approaches with surgery while sparing lung parenchyma.[1]

OBJECTIVES

To assess the safety and local recurrence-free survival in patients after cryoablation for treatment of pulmonary metastases. The primary objective was to evaluate the efficacy of cryoablation on local recurrence-free response (local tumor efficacy) for each index tumor at 12 months post-cryoablation after a single cryoablation procedure. The secondary endpoint was overall local tumor efficacy following a single or repeat cryoablation at 12 months. Separate evaluations of primary and secondary efficacy were also made for month 24. Safety data were captured for the incidence and severity of procedural adverse events.

METHODS

This multicenter, prospective, single-arm, phase 2 study included 128 patients with 224 lung metastases treated with percutaneous cryoablation, with 12 and 24 months of follow-up. Enrolled patients had pulmonary metastatic disease with one to six metastases with a maximal diameter of 3.5 cm. The primary objective was to evaluate the efficacy of cryoablation on local recurrence-free response (local tumor efficacy) for each index tumor at 12 months post-cryoablation after a single cryoablation procedure. Time to progression of the index tumor(s), metastatic disease, and overall survival rates were estimated using the Kaplan-Meier method. Complications were captured for 30 days after the procedure, and changes in performance status and quality of life were also evaluated.

The ablation procedure was performed under general anesthesia, conscious sedation, or regional anesthesia. CA needles, 1.5, 2.1 or 2.4 mm in diameter, were provided by Galil Medical Inc. (Arden Hills, MN) and placed under CT guidance. Cryoprobes were controlled with the Visual-ICE™ Cryoablation System.

Cryoablation was performed with a minimum of 3 freeze–thaw cycles (3-min freeze, 3-min passive thaw, 7-12 min freeze, 5-min passive thaw, 7-12 min freeze followed by active thawing). Each procedure was monitored with non-contrast CT imaging typically at 3 to 5 minutes intervals to visualize the evolving ablation zone with the goal of achieving a minimal margin beyond the tumor of 5mm. After CA needle(s) were removed, CT images were obtained to assess the overall ablation zone and to identify any potential complications. Follow-up was done within the first week, and at 1, 3, 6, 12, 18, and 24 months.

RESULTS

OUTCOMES

One hundred thirty patients with 226 tumors were treated with 169 CA procedures and included in the evaluation for complications. A total of 128 patients with 224 thoracic metastases treated over 167 procedures were included for the analysis of the efficacy. Of these patients, 80 of 224 tumors (36%) were treated with one cryoprobe and 144 (64%) of tumors were treated with two or more cryoprobes.

Initial and secondary efficacy is shown in Table 2. Initial local tumor efficacy (local recurrence-free survival) was achieved in 172/202 tumors (85.1%) (95% CI: 79.5, 89.8) after 12-months of follow-up and 139/180 (77.2%) (95% CI: 70.4, 83.1) after 24-months of follow-up. Time to progression, overall survival, time to progression from metastatic lung disease beyond the index tumor, and time to progression from metastatic disease were also evaluated. Kaplan-Meier estimates of 12- and 24-month overall survival rates were 97.6% (95% confidence interval: 92.6-99.2) and 86.6% (95% confidence interval: 78.7-91.7), respectively. Ten of the 128 patients treated (7.8%) received systemic therapies during the study. There were 3 and 12 deaths which occurred within 0-12, and 12-24 months respectively with no procedurally related deaths, 11 deaths related to disease progression and 4 unknowns.

Results found 77% primary and 84% secondary treatment efficacy at minimum of 24 months follow-up in patients achieving the primary endpoint with secondary treatment. In comparison, SBRT for the treatment of 50 patients with 125 metastatic pulmonary tumors resulted in 83% local efficacy at 18.7 months.[2]

COMPLICATIONS

Adverse events that occurred within 30 days of the procedure were captured and graded in accordance with the Common Terminology for Adverse Criteria for Adverse Events (CTCAE version 4.03) of the National Cancer Institute.(19) Changes in physical function and quality of life were measured using the Karnofsky Performance Scale (KPS), and the Short Form-12 (SF-12) assessment.(3) Pneumothoraces requiring intraprocedural pleural catheter placement occurred in 39/169 (23%) of procedures (captured as grade 2 adverse events). Pleural catheters were removed the next day in 9 of 44 (20.5%) of patients, within 2 days in an additional 23 patients (52.2%) of patients, and in 3 or more days in 12 (27.3%) patients. No patients required subsequent surgical treatment for bronchopleural fistula or for persistent pneumothorax. CTCAE grade 3 related adverse procedurally related events within 30 days of the procedure occurred in 8 of 169 (4.7%) procedures, including pneumothorax in 6 patients with pleural catheter placement in 5 of these patients, one pleural hemorrhage, and one hypoxic event. There were also one (0.6%) grade 4 event and no grade 5 events.

Cryoablation Treatment Characteristics

Characteristics	Value
Number of tumors	224
Number of procedures	167
Anesthesia	
General	115 (69%)
Conscious Sedation	49 (29%)
Local	3 (2%)
Mean number of needles per tumor diameter	
0.5-1.0cm	1.5±0.5
1.1-2.0cm	1.9±0.6
2.1-3.0cm	2.4±0.5
≥3.1cm	3.0±1.4
Median overall hospital stays, days (range)	1.0 (0-13)

Cryoablation Tumor Treatment Response at 12 and 24 months

Characteristic	Initial Treatment		Repeat Treatment		Secondary Treatment	
12-Month Interval	Response	Efficacy	Response	Efficacy	Response	Efficacy
Number of tumors	202	85.1%	12	100%	202	91.1%
Complete	33 (16.3%)		3 (20%)		36 (17.8%)	
Partial	122 (60.4%)		8 (66.7%)		130 (65.3%)	
Stable	17 (8.4%)		1 (13.3%)		18 (8.9%)	
Failure	30 (14.9%)		0 (0%)		18 (8.9%)	
24-Month Interval	Response	Efficacy	Response	Efficacy	Response	Efficacy
Number of tumors	180	77.2%	13	100%	180	84.4%
Complete	49 (37.2%)		7 (53.8%)		86 (47%)	
Partial	79 (43.9%)		7 (53.8%		86 (47.8%)	
Stable	11 (61%)		2 (15.4%)		13 (7.2%)	
Failure	41 (22.8%)		0 (0%)		28 (15.6%)	

CONCLUSION

Percutaneous cryoablation is a safe and effective treatment for pulmonary metastases in the largest prospective multi-center trial utilizing image-guided percutaneous cryoablation.

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