

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 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.

CONCLUSION

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

1. Dickinson KJ, Blackmon SH. Results of Pulmonary Resection: Colorectal Carcinoma. *Thorac Surg Clin.* 2016;26(1):41-7.

2. Okunieff P, Petersen AL, Philip A, Milano MT, Katz AW, Boros L, et al. Stereotactic Body Radiation Therapy (SBRT) for lung metastases. *Acta Oncol.* 2006;45(7):808-17.

3. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care.* 1996;34(3):220-33.

CRYOABLATION NEEDLES (IceSeed 1.5, IceSphere 1.5, IceSphere 1.5 CX, IceRod 1.5, IceRod 1.5 PLUS, IceRod 1.5 i-Thaw, IceRod 1.5 CX, IcePearl 2.1 CX and IceForce 2.1 CX) and ICEFX and VISUAL ICE CRYOABLATION SYSTEMS

INDICATIONS: The Galil Medical Cryoablation Needles and Systems are intended for cryoablative destruction of tissue during surgical procedures. The Cryoablation Needles, used with a Galil Medical Cryoablation System, are indicated for use as a cryosurgical tool in the fields of general surgery, dermatology, neurology (including cryoanalgesia), thoracic surgery (with the exception of cardiac tissue), ENT, gynecology, oncology, proctology, and urology. Galil Medical Cryoablation Systems are designed to destroy tissue (including prostate and kidney tissue, liver metastases, tumors and skin lesions) by the application of extremely cold temperatures. A full list of specific indications can be found in the respective Galil Medical Cryoablation System User Manuals. **CONTRAINDICATIONS:** There are no known contraindications specific to use of a Galil Medical Cryoablation Needle. **POTENTIAL ADVERSE EVENTS:** There are no known adverse events related to the specific use of the Cryoablation Needles. There are, however, potential adverse events associated with any surgical procedure. Potential adverse events which may be associated with the use of cryoablation may be organ specific or general and may include, but are not limited to abscess, adjacent organ injury, allergic/anaphylactoid reaction, angina/coronary ischemia, arrhythmia, atelectasis, bladder neck contraction, bladder spasms, bleeding/hemorrhage, creation of false urethral passage, creatinine elevation, cystitis, diarrhea, death, delayed/non healing, disseminated intravascular coagulation (DIC), deep vein thrombosis (DVT), ecchymosis, edema/swelling, ejaculatory dysfunction, erectile dysfunction (organic impotence), fever, fistula, genitourinary perforation, glomerular filtration rate elevation, hematoma, hematuria, hypertension, hypotension, hypothermia, idiosyncratic reaction, ileus, impotence, infection, injection site reaction, myocardial infarction, nausea, neuropathy, obstruction, organ failure, pain, pelvic pain, pelvic vein thrombosis, penile tingling/numbness, perirenal fluid collection, pleural effusion, pneumothorax, probe site paresthesia, prolonged chest tube drainage, prolonged intubation, pulmonary embolism, pulmonary insufficiency / failure, rectal pain, renal artery/renal vein injury, renal capsule fracture, renal failure, renal hemorrhage, renal infarct, renal obstruction, renal vein thrombosis, rectourethral fistula, scrotal edema, sepsis, skin burn/frostbite, stricture of the collection system or ureters, stroke, thrombosis/thrombus/embolism, transient ischemic attack, tumor seeding, UPJ obstruction/injury, urethral sloughing, urethral stricture, urinary fistula, urinary frequency/urgency, urinary incontinence, urinary leak, urinary renal leakage, urinary retention/oliguria, urinary tract infection, vaginal reaction, voiding complication including irritative voiding symptoms, vomiting, wound complication, and wound infection. PI-719210-AA

CRYOABLATION NEEDLES (IceSeed 1.5, IceSphere 1.5, IceSphere 1.5 CX, IceRod 1.5, IceRod 1.5 PLUS, IceRod 1.5 i-Thaw, IceRod 1.5 CX, IcePearl 2.1 CX and IceForce 2.1 CX) and ICEFX and VISUAL ICE CRYOABLATION SYSTEMS are registered or unregistered trademarks of Boston Scientific Corporation or its affiliates. All other trademarks are property of their respective owners.

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	
	Response	Efficacy	Response	Efficacy	Response	Efficacy
12-Month Interval						
Number of tumors	202		12		202	
Complete	33 (16.3%)	85.1%	3 (20%)	100%	36 (17.8%)	91.1%
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						
Number of tumors	180		13		180	
Complete	49 (37.2%)	77.2%	7 (53.8%)	100%	86 (47%)	84.4%
Partial	79 (43.9%)		7 (53.8%)		86 (47.8%)	
Stable	11 (6.1%)		2 (15.4%)		13 (7.2%)	
Failure	41 (22.8%)		0 (0%)		28 (15.6%)	

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