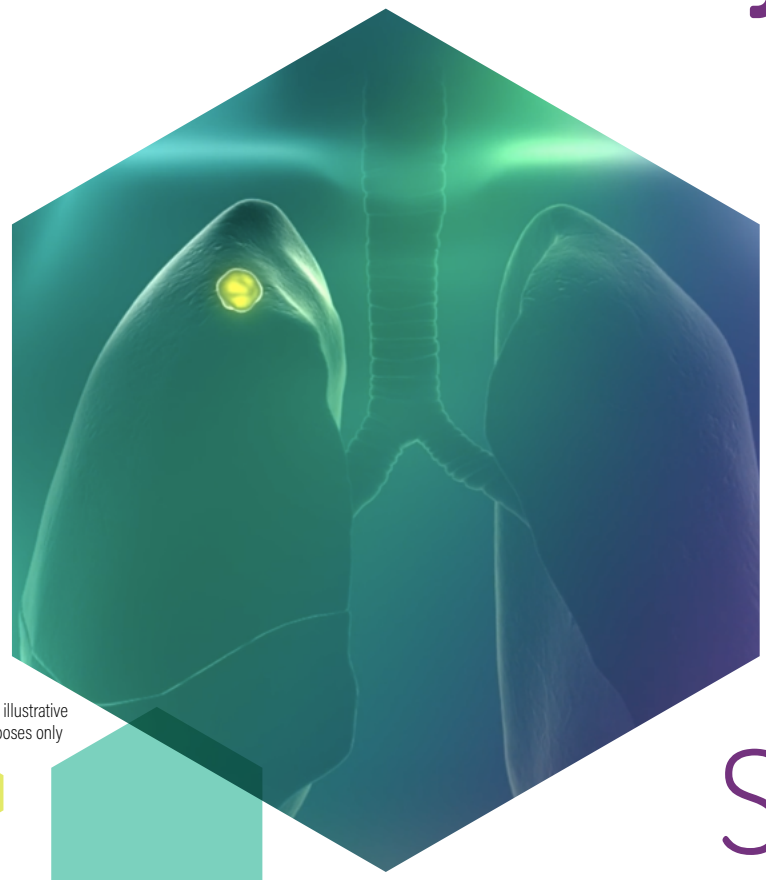
cytalux®
(pafolacianine) injection



*For illustrative purposes only

See Cancer in Real Time

CYTALUX® is the only IV-delivered molecular imaging agent that illuminates lung cancer intraoperatively for real-time localization of pulmonary lesions.

INDICATION AND USAGE

CYTALUX is an FDA approved optical imaging agent indicated as an adjunct for intraoperative identification of:

- Malignant lesions in adult patients with ovarian cancer.
- Malignant and non-malignant pulmonary lesions in adult patients with known or suspected cancer in the lung.

IMPORTANT SAFETY INFORMATION

RISK OF MISINTERPRETATION

Errors may occur with the use of CYTALUX during intraoperative fluorescence imaging to detect ovarian cancer and lesions in the lung, including false negatives and false positives. Non-fluorescing tissue in the surgical field does not rule out the presence of ovarian cancer or lesions in the lung. Fluorescence may be seen in normal tissues including bowel, kidneys, lymph nodes, lungs, and inflamed tissue.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

ONCTARGET LABORATORIES

Localizing small, deep, and subsolid lesions can be challenging.

Resection of small, deep or subsolid lesions can present unique challenges, particularly during parenchyma sparing operations. These lesions are often difficult to visualize and palpate, making precise localization a challenge.

> The inability to identify the lesion targeted for resection increases if the lesion is smaller than 10 mm or is located more than 5 mm from the pleural surface.[1]

Advancements in Technology

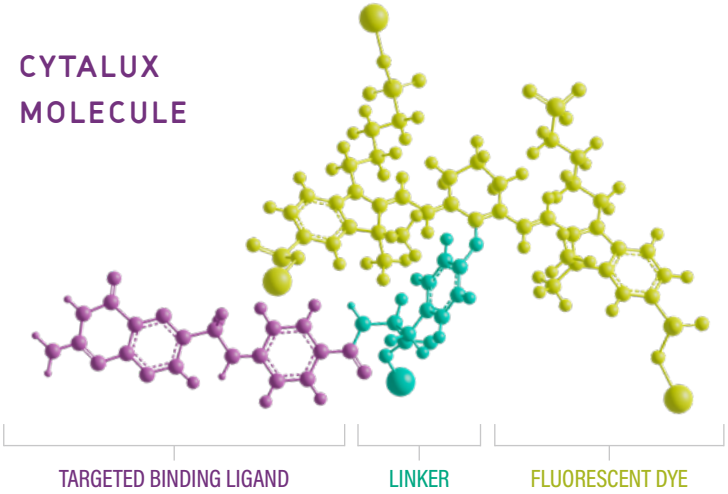
Existing preoperative localization methods require additional procedures for patients, which may increase cost and risk of complications. Coordinating these additional procedures can be challenging and delay the patient's surgical procedure. In addition, technical challenges with existing localization options can yield imprecise results, such as spreading of dyes, dislodging of wires, and inaccurate placement.

> Newer, more targeted molecular imaging agents are being developed to fluoresce cancer in real time during surgery without requiring additional procedures for the patient.

MECHANISM OF ACTION

CYTALUX®: The Only Targeted Intraoperative Molecular Imaging Agent That Illuminates Lung Cancer In Real Time

CYTALUX MOLECULE



FOLATE

- Folate is an essential vitamin **required for cell growth** and DNA replication.[2]
- Rapidly dividing cancer cells require an abundant supply of folate, therefore, it is **consumed in elevated quantities**.[2]
- Folate receptor-alpha expression has been demonstrated to be present in **86% of pulmonary adenocarcinomas**.[3]

HOW CYTALUX WORKS

1. CYTALUX is a small molecule that circulates quickly through the body.
   - It can be infused intravenously in as little as an hour before surgery.
2. CYTALUX binds to the folate receptors expressed on cells.
   - It is targeted, preferentially binding to FR+ cells.
3. CYTALUX is endocytosed and concentrates in folate receptor positive (FR+) lung cancer tissues.
   - Endocytosis allows it to be concentrated in the tissues throughout the surgical procedure.
4. CYTALUX contains a bright fluorophore which is illuminated via near-infrared light.
   - Imaging under near-infrared light enhances intraoperative visualization in challenging environments and below the tissue surface.[3]

IMPORTANT SAFETY INFORMATION

INFUSION-RELATED REACTIONS

Adverse reactions including nausea, vomiting, abdominal pain, flushing, hypersensitivity, elevation in blood pressure, dyspepsia, and chest discomfort were reported in patients receiving CYTALUX in clinical studies. A total of 17% of patients experienced reactions during administration of CYTALUX. Reactions typically occurred within 15 minutes of the start of infusion. CYTALUX infusion interruption or discontinuation due to adverse reactions occurred in 11% of all patients. Treatment with antihistamines and/or anti-nausea medication may be used. If an adverse reaction occurs during administration, the infusion can be interrupted and resumed after treatment of the reaction.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

For more information or to request to speak with a sales representative visit www.cytaluxhcp.com

cytalux® (pafolacianine) injection

ELUCIDATE: Enabling Lung Cancer Identification Using Folate Receptor Targeting

A Phase 3, randomized, single dose, open-label trial that investigated the safety and efficacy of CYTALUX® for intraoperative imaging of folate receptor positive lung lesions.

Patients undergoing surgical resection for lung cancer

Patient infused with CYTALUX
1–24 hours prior to surgery
N=112

Lesions identified under conventional white light and palpation

Randomization
Patient served as own control

No intraoperative molecular imaging
N=11

Evaluation under intraoperative molecular imaging with CYTALUX
N=100

Margin measured on back table

Surgical field reinspected for synchronous lesions

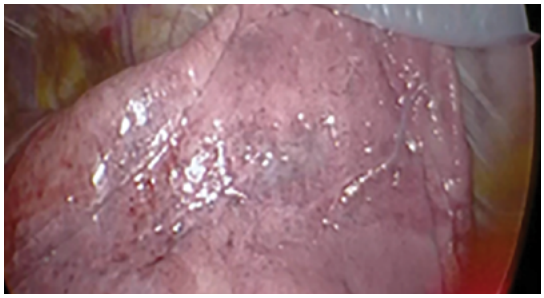
Resected lesions evaluated by pathologist

Primary Endpoint

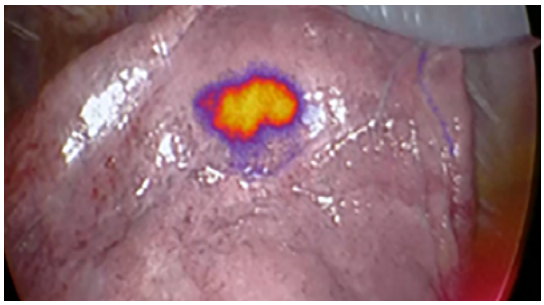
Proportion of patients with one or more Clinically Significant Event (CSE).

Three Types of CSEs

- Localization of primary lesion
- Detection of one or more synchronous malignant lesions
- Identification of close resection margin



view with white light only



CYTALUX with near-infrared imaging

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CYTALUX® detected additional lung cancer in a Phase 3 Trial

cytalux® (pafolacianine) injection

In **19%** of patients, the primary lung lesion was localized, but not detected with conventional methods.

In **8%** of patients, one or more synchronous malignant lesions not detected by preoperative imaging was identified.

In **38%** of patients, a close resection margin (≤10mm) was identified.*

Surgeons indicated a change in scope of their procedure in **29%** of patients.†

CYTALUX did not identify the primary lung lesion in 23% (95% CI [15-32]) of patients. Among the 20 patients who had synchronous lesions detected only by CYTALUX, 12 patients had only benign synchronous lesions.

* Phase 3 (007 Study): CYTALUX FOR FR+ LUNG CANCER; N=38/100, (38%, 95% CI [28.5-48.3]). The clinically significant event (CSE) for margin was one of three pre-defined CSE categories making up the primary endpoint for the purposes of the ELUCIDATE trial only and thus are not part of the label indication so therefore should be interpreted cautiously. Sarkaria IS, Martin LW, Rice DC, Blackmon SH, Slade HB, Singhal S; ELUCIDATE Study Group. Pafolacianine for intraoperative molecular imaging of cancer in the lung: The ELUCIDATE trial. J Thorac Cardiovasc Surg. 2023 Mar 3:S0022-5223(23)00185-X. doi: 10.1016/j.jtcvs.2023.02.025. Epub 2023 Mar 02. PMID: 37019717

† Based on a prespecified exploratory endpoint for the proportion of subjects for whom the surgical plan was changed based on fluorescence imaging both prior to initiation of the surgical procedure and upon re-imaging of the surgical field after surgical procedure prior to closing. (N=100, 95% CI [20.4, 38.9])

LESION SIZE

SIZE OF LESIONS IDENTIFIED BY CYTALUX AND NOT BY STANDARD WHITE LIGHT IN PHASE 3 STUDY*	MEDIAN	MINIMUM
Primary lesions	13 mm	5 mm
Synchronous lesions	12 mm	2 mm

*as measured by local pathology

LESION DEPTH

DEPTH OF LESIONS DETECTED BY CYTALUX IN PHASE 3 STUDY*	MEDIAN	MAXIMUM
Detected by CYTALUX only	11.5 mm	27.9 mm
Detected by CYTALUX and white light	4.3 mm	37.7 mm

*As measured by preoperative CT/PET imaging. The depth of primary lung lesions detected by CYTALUX ranged from 0 to 38 mm from the lung surface (mean depth 6 mm).

Drug-Related Adverse Events

ELUCIDATE Phase 3 Trial N=112 study subjects infused with CYTALUX

DRUG-RELATED ADVERSE EVENTS	MILD/MODERATE n (%)	SEVERE n (%)
Subjects with at least one drug-related TEAE*	36 (32.1%)	3 (2.7%)
Total number of drug-related TEAEs*	55	5

MOST COMMON (>2%) DRUG-RELATED ADVERSE EVENTS	MILD/MODERATE n (%)	SEVERE n (%)
Nausea	10 (8.9%)	0
Vomiting	4 (3.6%)	0
Intermittent hypertension	3 (2.7%)	1 (0.9%)

* TEAE = Treatment Emergent Adverse Event

ZERO drug-related serious adverse events were observed in any patient dosed with CYTALUX.

92% of all drug-related adverse events were mild-to-moderate.

Workflow Integration

cytalux® (pafolacianine) injection

CYTALUX® seamlessly integrates in the perioperative surgical process.

PREPARE
the recommended dose of CYTALUX as a single intravenous infusion.

ADMINISTER
CYTALUX during a 60-minute infusion, 1 to 24 hours prior to surgery for lung cancer.

ILLUMINATE
lung cancer lesions intraoperatively using a near-infrared imaging system cleared for use with CYTALUX.

A near-infrared imaging system is used to illuminate CYTALUX

- Clinical data demonstrates NIR imaging devices which excite at 760nm to 785 nm and detect emission at 790 nm to 815 nm are suitable for use with CYTALUX.
- CYTALUX is to be used with a near-infrared (NIR) imaging system cleared by FDA for specific use with pafolacianine.
- CYTALUX should only be used by surgeons who have completed a training program on the use of NIR imaging systems for fluorescence imaging during surgery. Training is provided by the device manufacturer.

*For illustrative purposes only

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

The safety of CYTALUX was evaluated in four open label clinical studies, two studies (N = 44 and N = 150) in patients with ovarian cancer and two studies (N = 100 and N = 112) in patients with known or suspected cancer in the lung. A total of 406 patients received 0.025 mg/kg of CYTALUX via intravenous administration.

Adverse reactions that occurred in ≥ 1% of patients were: nausea (13%), vomiting (5%), abdominal pain (2%), flushing (2%), other infusion-related reactions (2%), hypersensitivity (2%), elevation in blood pressure (1%), dyspepsia (1%), and chest discomfort (1%). Adverse reactions occurred during the administration of CYTALUX in 17% of patients.

EMBRYO-FETAL TOXICITY

Based on its mechanism of action, CYTALUX may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to a fetus. Verify pregnancy status of females of reproductive potential prior to initiating CYTALUX treatment.

RISK OF PAFOLACIANINE AGGREGATION AND INFUSION REACTIONS

Use of the incorrect diluent to prepare the CYTALUX infusion solution can cause the aggregation of pafolacianine; aggregation may induce infusion reactions such as nausea, vomiting, abdominal pain or rash. Use only 5% Dextrose Injection to prepare the CYTALUX infusion solution. Do not use other diluents.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

REFERENCES

1 Suzuki K, Nagai K, Yoshida J, Ohmatsu H, Takahashi K, Nishimura M, Nishiwaki Y. Videoassisted thoracoscopic surgery for small indeterminate pulmonary nodules: indications for preoperative marking. Chest. 1999 Feb;115(2):563-8. doi: 10.1378/chest.115.2.563. PMID:10027460.

2 Markert S, et al. Alpha-folate receptor expression in epithelial ovarian carcinoma and non-neoplastic ovarian tissue. Anticancer Res. 2008 (28): 3568-3572.

3 Predina JD, Newton AD, Connolly C, Dunbar A, Baldassari M, Deshpande C, Cantu E 3rd, Stadanlick J, Kularatne SA, Low PS, Singhal S. Identification of a Folate Receptor-Targeted Near-Infrared Molecular Contrast Agent to Localize Pulmonary Adenocarcinomas. Mol Ther. 2018 Feb 7;26(2):390-403. doi: 10.1016/j.ymthe.2017.10.016. Epub 2017 Oct 26. PMID: 29241970; PMCID: PMC5835020.

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