

\*For illustrative purposes only

**cytalux**<sup>TM</sup>  
(pafolacianine) injection



# Real-Time Cancer Imaging

Introducing the latest advancement in Intraoperative Molecular Imaging that makes ovarian cancer visible in real time.

## INDICATION AND USAGE

CYTALUX<sup>TM</sup> is an FDA-approved optical imaging agent indicated in adult patients with ovarian cancer as an adjunct for intraoperative identification of malignant lesions.

## IMPORTANT SAFETY INFORMATION

### RISK OF MISINTERPRETATION

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

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

ON  TARGET  
LABORATORIES

# A Complete Resection is the Goal of Treatment for Ovarian Cancer

The amount of gross residual disease after cytoreductive surgery in ovarian cancer patients has been demonstrated to be an important independent predictor of clinical outcomes.<sup>1</sup> However, debulking surgery in women with advanced stage ovarian cancer often results in suboptimal outcomes.

Studies show that among patients reported to have undergone optimal cytoreduction, 40% were found to have measurable disease on 30-day postoperative imaging.<sup>2</sup>

## Advancements in Technology

Currently, visual inspection and palpation during surgery are the main tools utilized to estimate the extent of tumor involvement and to guide debulking. Fluorescence-Guided Surgery is an imaging technique that uses fluorescent dye to identify anatomic structures during surgical procedures using a near-infrared imaging system.

Newer, more targeted technologies are being developed to improve intraoperative visualization of cancerous tissue.



## MECHANISM OF ACTION

# CYTALUX™: The First Targeted Intraoperative Molecular Imaging Agent That Illuminates Ovarian Cancer In Real Time

### FOLATE

Folate is an essential vitamin **required for cell growth** and DNA replication<sup>3</sup>

Rapidly dividing cancer cells requires an abundant supply of folate, therefore, it is **consumed in elevated quantities**<sup>3</sup>

Most ovarian cancers overexpress high-affinity folate receptors to **increase folate uptake for tumor growth**<sup>4</sup>

### HOW CYTALUX WORKS

CYTALUX is a small molecule that circulates quickly through the body

It can be infused intravenously in as little as an hour before surgery

CYTALUX binds to the folate receptors on ovarian cancer cells

It is targeted, preferentially binding to FR+ ovarian cancer cells

CYTALUX is endocytosed and concentrates in folate receptor positive (FR+) ovarian cancer tissues

Endocytosis allows it to be concentrated in the tissues throughout the surgical procedure

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<sup>5</sup>

## IMPORTANT SAFETY INFORMATION

### INFUSION-RELATED REACTIONS

Adverse reactions consisting of nausea, vomiting, abdominal pain, flushing, dyspepsia, chest discomfort, and pruritus were reported in patients receiving CYTALUX in clinical studies. 2.4% of patients experienced reactions during the period of administration of CYTALUX. Reactions typically occurred within 15 minutes of the start of infusion. 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.

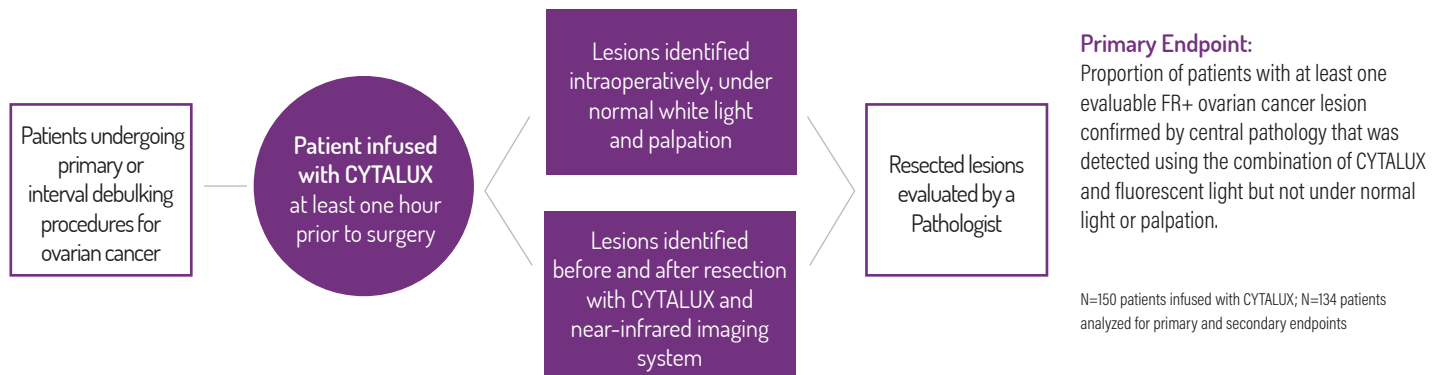
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# CYTALUX™ Detected Additional Ovarian Cancer which would have been left behind

## PHASE 3 (006 STUDY): CYTALUX FOR FR+ OVARIAN CANCER

A Phase 3, Randomized, Single Dose, Open-Label Study to Investigate the Safety and Efficacy of CYTALUX for Intraoperative Imaging of Folate Receptor Positive Ovarian Cancer



**WITH CYTALUX, ADDITIONAL LESIONS WERE FOUND IN 27% OF PATIENTS\***

\* Women highly suspicious for or with confirmed ovarian cancer who underwent both normal and fluorescent light evaluation (Intent-to-Image set); N=134, 95% CI [19.6, 35.2]

In a subgroup analysis of patients with confirmed FR+ ovarian cancer who underwent interval debulking surgery

**ADDITIONAL LESIONS WERE FOUND IN 40% OF INTERVAL DEBULKING PATIENTS\*\***

\*\* Phase 3 (006 Study): CYTALUX FOR FR+ OVARIAN CANCER; N=58, 95% CI [27.0, 53.4]  
This subgroup analysis utilized a smaller analysis set than the primary endpoint and was not adjusted to control for error, so the results are not conclusive and should be interpreted cautiously.

Patient-level false positive rate with respect to the detection of ovarian cancer lesions confirmed by central pathology was 20%; 95% CI [0.137, 0.280]

## Drug-Related Adverse Events Phase 3 (006 Study): CYTALUX FOR FR+ OVARIAN CANCER N=150 study subjects infused with CYTALUX

DRUG-RELATED ADVERSE EVENT	MILD/MODERATE n (%)	SEVERE n (%)
Subjects with at least one drug-related TEAE	43 (28.7%)	2 (1.3%)
Total number of drug-related TEAEs	63	2

MOST COMMON DRUG-RELATED ADVERSE EVENTS	MILD/MODERATE n (%)	SEVERE n (%)
Nausea	27 (18.0%)	0
Vomiting	8 (5.3%)	0
Abdominal Pain	7 (4.7%)	0

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

**97%** of all drug-related adverse events were mild-to-moderate.

# Workflow Integration

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 9 hours prior to surgery

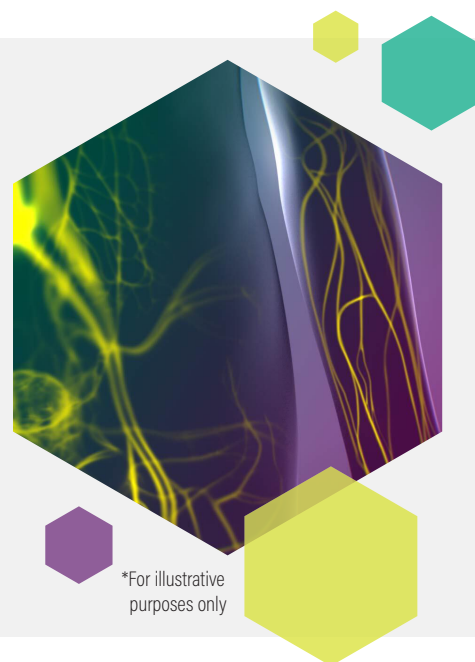


## ILLUMINATE

ovarian cancer lesions intraoperatively using a near-infrared imaging system cleared for use with CYTALUX

## A near-infrared imaging system is used to illuminate CYTALUX

- ▶ CYTALUX is to be used with a near-infrared imaging system (NIR) cleared by the FDA for specific use with CYTALUX
- ▶ Clinical data demonstrates that NIR imaging devices which excite at 760 nm to 785 nm and detect emission at 794 nm to 796 nm are suitable for use with CYTALUX
- ▶ 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



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## IMPORTANT SAFETY INFORMATION

### 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

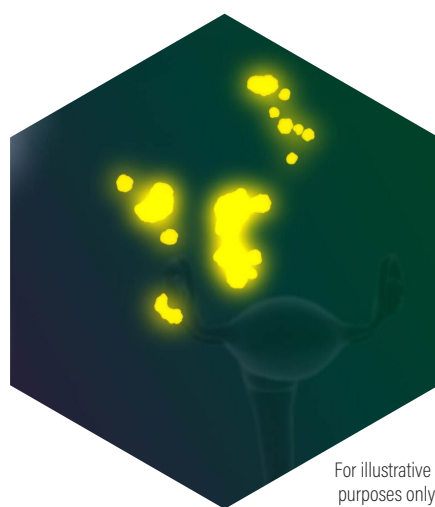
Use of the incorrect diluent to prepare the CYTALUX infusion solution can cause the aggregation of pafolacianine; aggregation may induce infusion reactions such as nausea, vomiting, abdominal pain or rash. Use only 5% Dextrose Injection to prepare the CYTALUX infusion solution. Do not use other diluents.

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The use of  
CYTALUX helped  
surgeons detect additional  
cancer which would have  
otherwise been left behind  
in 27% of patients.\*

## CYTALUX™ Gives You An Advantage

CYTALUX is the first targeted intraoperative molecular imaging agent that illuminates ovarian cancer in real time, enabling the detection of more cancer for resection.

\*Women highly suspicious for or with confirmed ovarian cancer who underwent both normal and fluorescent light evaluation (Intent-to-Image set); N=134, 95% CI [0.196, 0.352]

**Folate receptors  
are overexpressed**  
in most ovarian cancers.<sup>4</sup>

**CYTALUX binds to  
folate receptors and is  
fluoresced intraoperatively**  
using a near-infrared  
imaging system.

Surgeons indicated the  
use of CYTALUX **altered  
their surgical plan in  
54% of their cases.**<sup>\*\*</sup>

<sup>\*\*</sup> Phase 3 (006 Study): Based on a prespecified exploratory endpoint for the proportion of subjects for whom the fluorescence 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=109, 95% CI [44.3, 63.7])

### INDICATION AND USAGE

CYTALUX™ is an FDA-approved optical imaging agent indicated for adult patients with ovarian cancer as an adjunct for intraoperative identification of malignant lesions.

### IMPORTANT SAFETY INFORMATION

#### ADVERSE REACTIONS

Adverse reactions that occurred in > 1 % of patients were: nausea (15%), vomiting (5.8%), abdominal pain (2.7%), flushing (1.7%), dyspepsia (1%), chest discomfort (1%), pruritus (1%) and hypersensitivity (1%).

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## REFERENCES

- <sup>1</sup> Chang SJ, Hodeib M, Chang J, Bristow RE. Survival impact of complete cytoreduction to no gross residual disease for advanced-stage ovarian cancer: a meta-analysis. *Gynecol Oncol*. 2013 Sep;130(3):493-8. doi: 10.1016/j.jygyno.2013.05.040. Epub 2013 Jun 6. PMID: 23747291.
- <sup>2</sup> Eskander RN, Kauderer J, Tewari KS, Mannel RS, Bristow RE, O'Malley DM, Rubin SC, Glaser GE, Hamilton CA, Fujiwara K, Huh WK, Ueland F, Stephan JM, Burger RA. Correlation between Surgeon's assessment and radiographic evaluation of residual disease in women with advanced stage ovarian cancer reported to have undergone optimal surgical cytoreduction: An NRG Oncology/Gynecologic Oncology Group study. *Gynecol Oncol*. 2018 Jun;149(3):525-530. doi: 10.1016/j.jygyno.2018.03.043.
- <sup>3</sup> Markert S, et al. Alpha-folate receptor expression in epithelial ovarian carcinoma and non-neoplastic ovarian tissue. *Anticancer Res*. 2008 (28): 3568-3572.
- <sup>4</sup> Kalli KR, Oberg AL, Keeney GL, et al. Folate receptor alpha as a tumor target in epithelial ovarian cancer. *Gynecologic Oncology*. 2008;108(3):619-626.
- <sup>5</sup> 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.jymthe.2017.10.016. Epub 2017 Oct 26. PMID: 29241970; PMCID: PMC5835020.