



Fluorescence-guided surgery (FGS) using pafolacianine
Ovarian and Lung Indications
ICD-10 Coordination and Maintenance Committee Meeting

March 7, 2023

CYTALUX® FDA APPROVAL - OVARIAN AND LUNG CANCER



OVARIAN CANCER

20,000 women are diagnosed with ovarian cancer every year in the U.S.¹

#1 cause of gynecologic cancer deaths¹

70% of patients diagnosed with ovarian cancer will have a recurrence²



LUNG CANCER

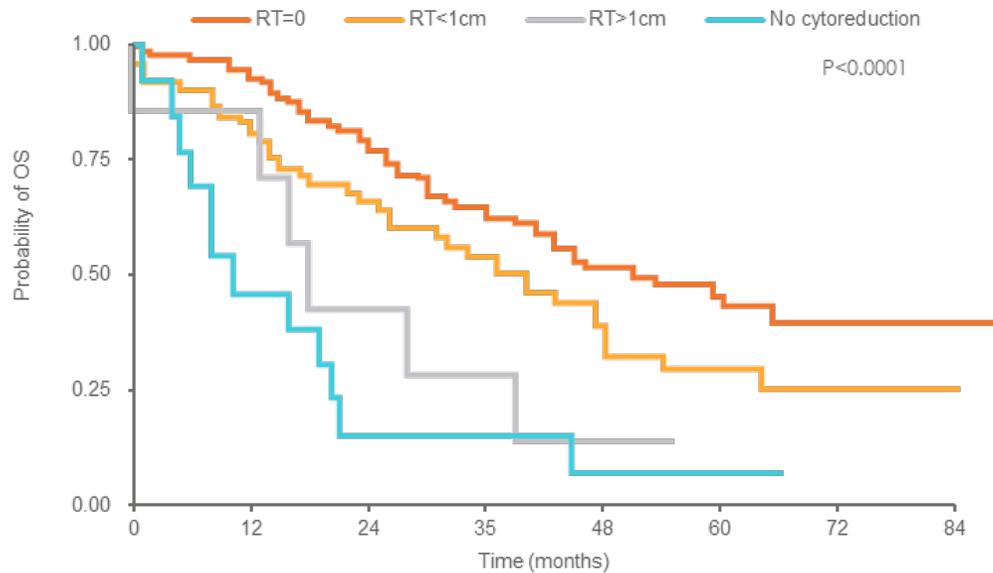
237,000 people are diagnosed with lung cancer every year in the U.S.³

#1 cause of cancer deaths³

30-55% of patients who undergo surgical resection develop a recurrence and do not survive⁴ and up to **24% recur locally**⁵

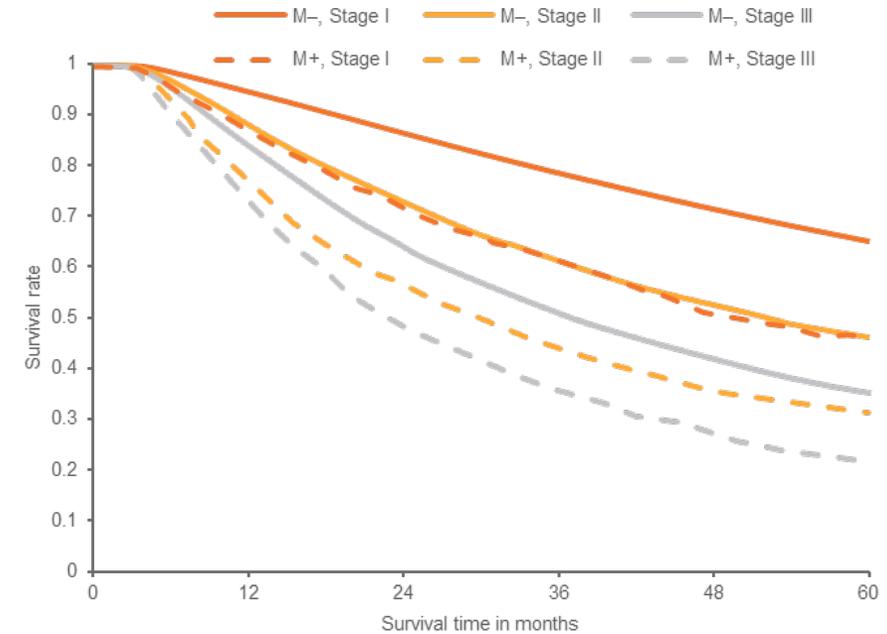
COMPLETE RESECTIONS ARE ASSOCIATED WITH IMPROVED SURVIVAL

OVARIAN CANCER 5YR OVERALL SURVIVAL AFTER SURGERY BY RESIDUAL DISEASE⁶



- R0 (*no evidence of disease*) resection resulted in the best survival
- Steep drop in survival with residual tumor >1cm remaining following cytoreductive surgery

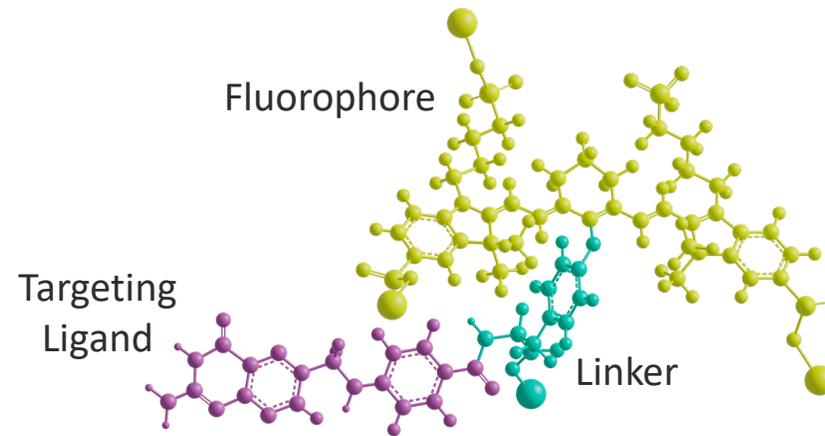
LUNG CANCER 5YR OVERALL SURVIVAL AFTER SURGERY BY RESECTION MARGIN⁷



- Positive margin after lung resection resulted in worse survival compared to negative margin

CYTALUX[®] MECHANISM OF ACTION, ADMINISTRATION, MEDICAL RECORD DOCUMENTATION

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



MECHANISM OF ACTION

- **Infused intravenously** and circulates quickly through the body
- Preferentially **binds to folate receptors**, which are overexpressed on most ovarian (72-97%^{8,9}) and lung cancer (86%¹⁰) cells
- **Endocytosed and concentrates** in folate receptor positive ovarian and lung cancer tissues
- **Illuminated during surgery** via near-infrared light

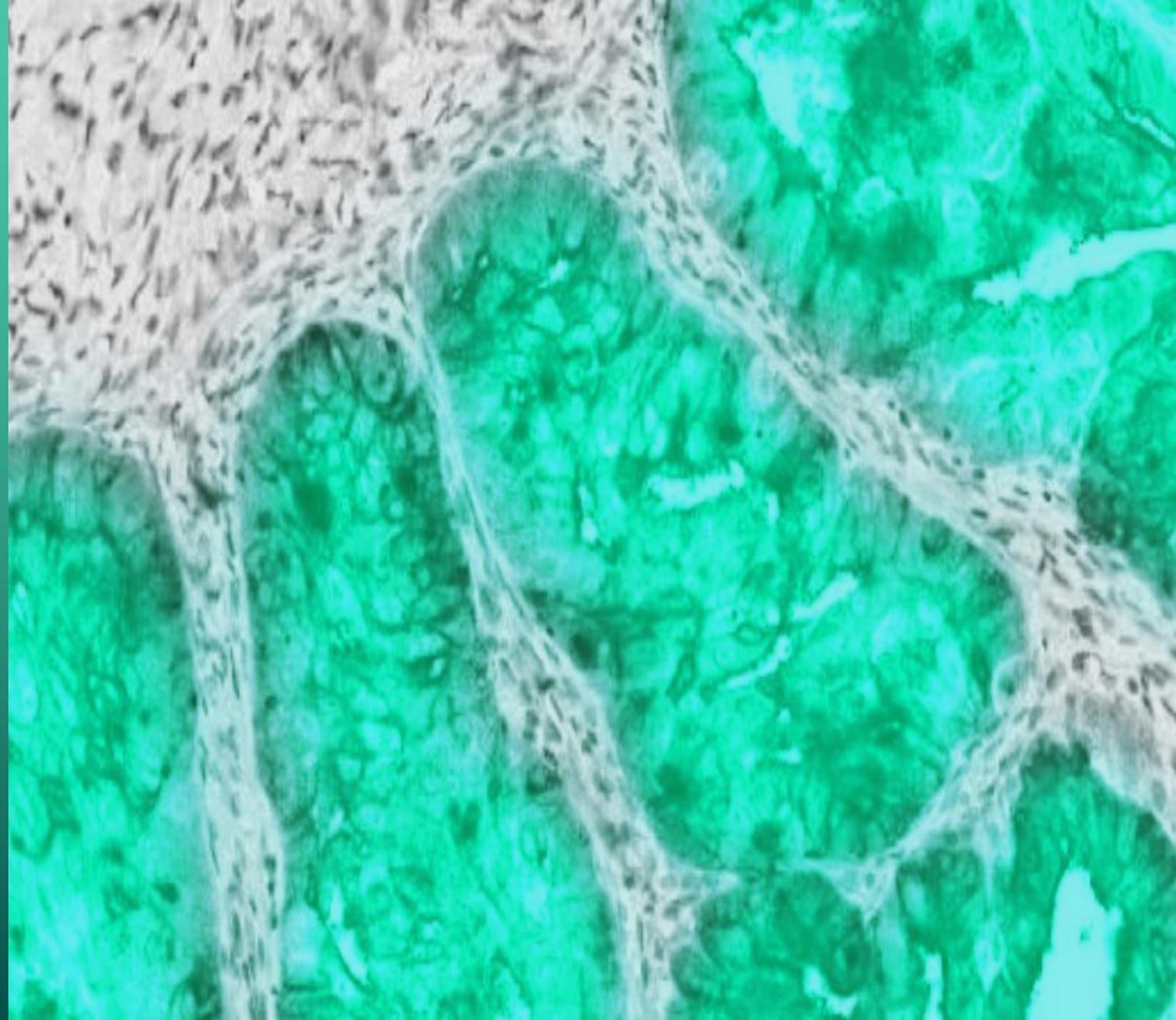
DOSAGE & ADMINISTRATION

- The recommended dose of CYTALUX[®] is a single intravenous **infusion of 0.025 mg/kg** diluted in 250mL of 5% Dextrose Injection
- Infused **over 60 minutes** using a dedicated infusion line
- Administered **1 hour to 9 hours prior to surgery (Ovarian); 1 hour to 24 hours prior to surgery (Lung)**

MEDICAL RECORD DOCUMENTATION

CYTALUX[®] documentation would be found in the Medication Administration Record (MAR), surgical or operative report and/or progress notes

CYTALUX® FOR OVARIAN CANCER



CYTALUX[®] FDA APPROVED FOR OVARIAN CANCER NOVEMBER 29, 2021

OVARIAN CANCER INDICATION

CYTALUX[®] is indicated as an adjunct for intraoperative identification of malignant lesions in adult patients with ovarian cancer.

Received **Orphan, Fast Track and Priority Review** designations, demonstrating significant unmet need

UNMET NEED IN OVARIAN CANCER

IMPORTANCE OF ACHIEVING COMPLETE CYTOREDUCTION

- Patient **survival is greater** among patients who receive complete cytoreduction⁶
- The **amount of residual disease** is an independent prognostic factor of survival, and the absence of macroscopic residual disease is associated with a **significantly lower risk of recurrence**¹¹
- In a retrospective study of 496 patients, those with residual disease of 1-10mm had **better progression-free survival and overall survival** than patients with residual disease >10mm¹²
- Use of **visual inspection and palpation** to identify ovarian cancer lesions may not be enough to achieve complete cytoreduction¹³



Traditional view of operating field with current tools of white light visualization and palpation



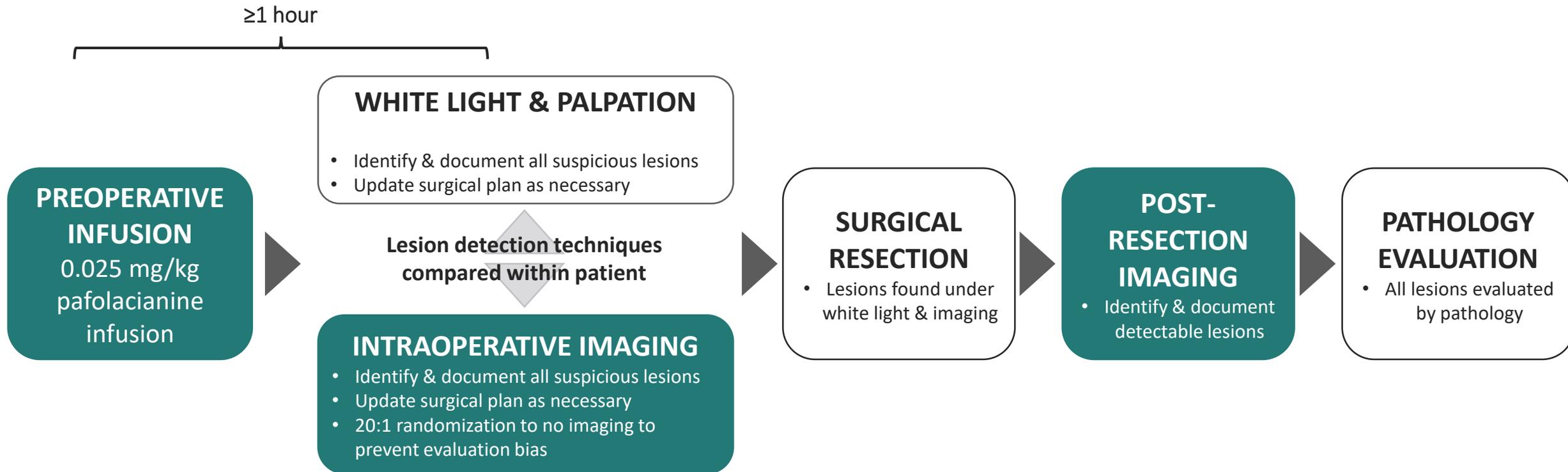
Enhanced visualization with CYTALUX and near-infrared imaging

OVARIAN CANCER: 006 TRIAL PHASE 3 TRIAL DESIGN

Open-label, Single-dose, Prospective Trial

N=150 patients infused with pafolacianine

N=134 patients analyzed for primary and secondary endpoints in Intent-to-Image Set (ITI)



006 TRIAL: DEMOGRAPHICS AND OVARIAN CANCER CHARACTERISTICS

	N (%)
N	150
Age, mean	60.8
Ethnicity, % Hispanic/Latino	18 (12.0)
Race, %	
American Indian or Alaska Native	4 (2.7)
Asian	7 (4.7)
Black or African American	7 (4.7)
Native Hawaiian or Other Pacific Islander	0 (0)
White	127 (84.7)
Other	4 (2.7)
Not reported	1 (0.7)
Childbearing Potential, %	
Potentially able to bear children	23 (15.3)
Post-menopausal	127 (84.7)

	N (%)
	109
Stage at Diagnosis	
I	7 (6.5)
II	8 (7.3)
III	73 (67.0)
IV	17 (15.6)
Unknown	4 (3.7)
Histological Epithelial Cell Type	
Serous adenocarcinoma	90 (82.6)
Endometrioid carcinoma	3 (2.8)
Undifferentiated adenocarcinoma	7 (6.4)
Clear cell adenocarcinoma	4 (3.7)
Other	5 (4.6)

006 TRIAL: SAFETY AND TOLERABILITY

Most frequently reported infusion-related reactions

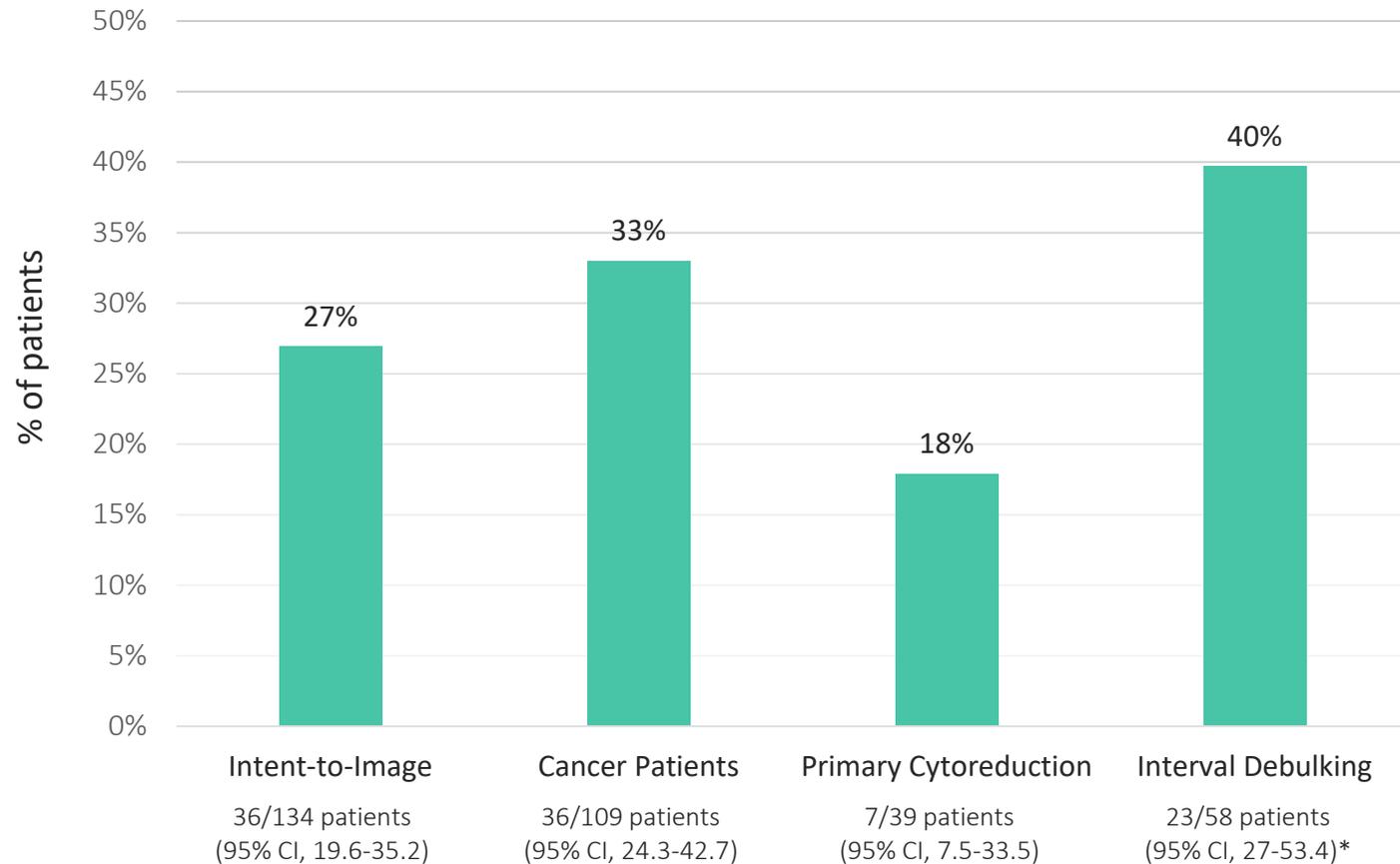
	Mild N (%)	Moderate N (%)	Severe N (%)
Subjects with at least 1 TEAE	30 (20.0)	13 (8.7)	2 (1.3)
Total number TEAEs	45	18	2
Nausea	18 (12.0)	9 (6.0)	0
Vomiting	4 (2.7)	4 (2.7)	0
Abdominal pain	5 (3.3)	2 (1.3)	0
Dyspepsia	2 (1.3)	0	0
Anemia	0	0	2 (1.3)

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

No drug-related serious adverse events

006 TRIAL PRIMARY ENDPOINT: PERCENT OF PATIENTS ADDITIONAL OVARIAN CANCER WAS FOUND WITH CYTALUX[®]

Patients (%) with ≥ 1 FR-positive ovarian cancer lesion detected by intraoperative molecular imaging but not by normal white light/palpation on tissue not planned for resection



- **Confirmed by blinded central pathology**
- **Located on tissue not planned for resection**
- **Detected by CYTALUX[®] with near-infrared imaging**
- **Not detected by normal white light and palpation alone**

006 TRIAL: INVESTIGATOR REPORTED OUTCOMES

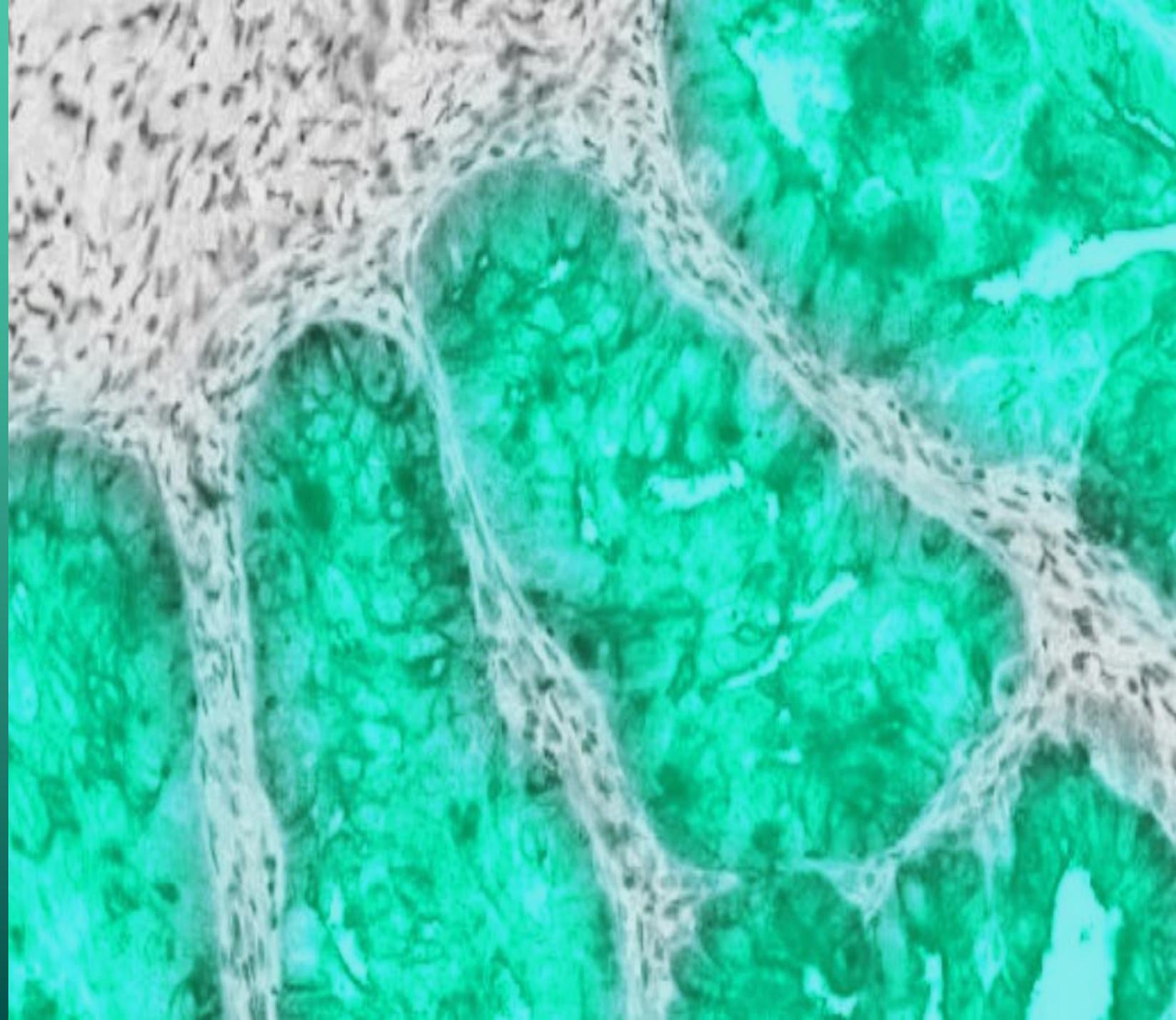
In a post-procedural questionnaire (n=109), investigators reported information gained from use of pafolacianine with near-infrared imaging yielded the following:

56% of patients: surgical plan was revised due to use of CYTALUX®

51% of patients: more complete debulking achieved

62% of patients: complete resection (R0) achieved

CYTALUX® FOR LUNG CANCER



CYTALUX[®] FDA APPROVED FOR LUNG CANCER DECEMBER 16, 2022

LUNG CANCER INDICATION

CYTALUX[®] is indicated as an adjunct for intraoperative identification of malignant and non-malignant pulmonary lesions in adult patients with known or suspected cancer in the lung.

Received **Fast Track** and **Priority Review** designations, demonstrating significant unmet need

UNMET MEDICAL NEED IN CANCER OF THE LUNG

- Five-year **survival for early-stage lung cancer remains low** at 61.2% for localized disease and 33.5% for regional disease¹⁴
- **30-55% of patients have a recurrence** following lung cancer surgery, with up to 24% of patients recurring locally
- Average **survival following local recurrence is less than one year**¹⁵
- One study showed **8-9% of patients had malignant synchronous lesions** not identified by preoperative CT imaging¹⁶
- **Increased margin is associated with a lower risk of local recurrence**; a 10mm margin has a 45% lower recurrence risk than 5mm¹⁷
- During minimally invasive thoracic surgery, **smaller and deeper nodules are not always able to be located**¹⁸



Traditional view of operating field with current tools of white light visualization and palpation



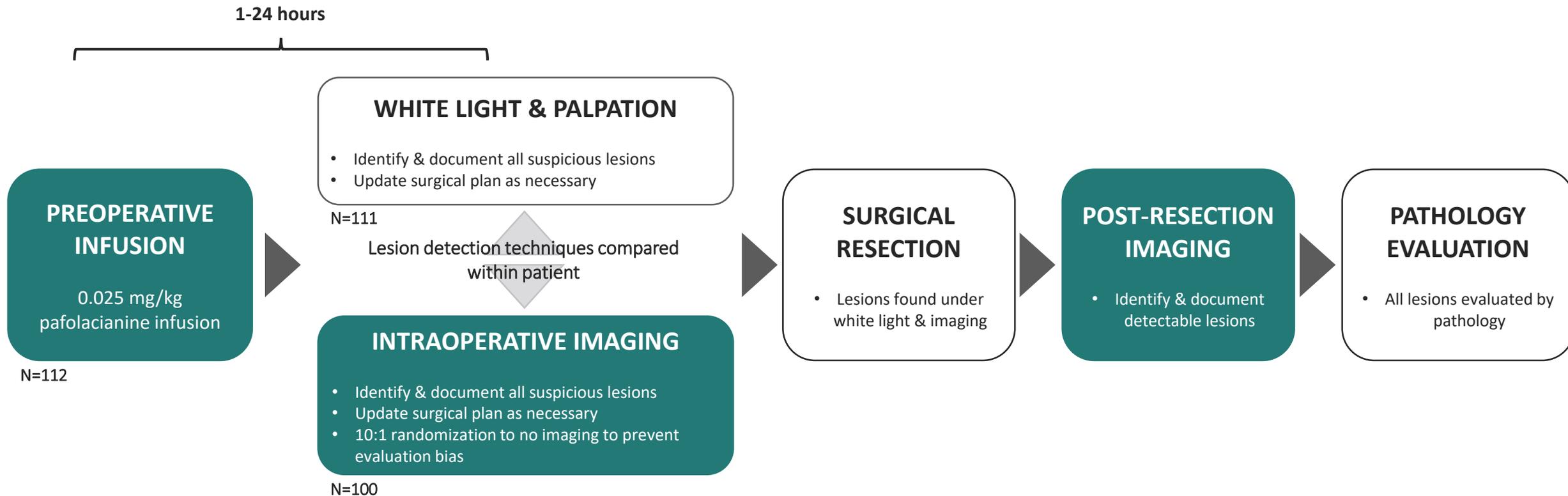
Enhanced visualization with CYTALUX® and near-infrared imaging

LUNG CANCER: ELUCIDATE 007 TRIAL PHASE 3 TRIAL DESIGN

Open-label, Single-dose, Prospective Trial

N=112 patients infused with pafolacianine

N=100 patients analyzed for primary and secondary endpoints in Full Analysis Set (FAS)



ELUCIDATE TRIAL: DEMOGRAPHICS AND LUNG CANCER PROCEDURE CHARACTERISTICS

		N (%)
Sex	Male	39 (39.0)
	Female	61 (61.0)
Age	Mean	66
	Min, Max	26, 83
Race	Asian	2 (2.0)
	Black	8 (8.0)
	White	88 (88.0)
	Other	2 (2.0)
Smoking History	Current	19 (19.0)
	Former	52 (52.0)
	Never	29 (29.0)

		N (%)
Histology	Adenocarcinoma	65 (73.0)
	Squamous Cell	7 (7.9)
	Metastatic Cancers	17 (19.1)
Procedure	Wedge Resection	72 (72.0)
	Segmentectomy	15 (16.0)
	Lobectomy	12 (12.0)
	No Resection	1 (1.0)
Robotic	Robotic	49 (49.0)
	VATS	51 (51.0)

ELUCIDATE TRIAL: SAFETY AND TOLERABILITY

Most frequently reported infusion-related reactions

	N (%)
Nausea	10 (8.9)
Intermittent Hypertension	4 (3.6)
Vomiting	4 (3.6)
Upper Abdominal Pain	2 (1.8)
Flushing	2 (1.8)
Transient Hypotension	2 (1.8)

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

No drug-related serious adverse events

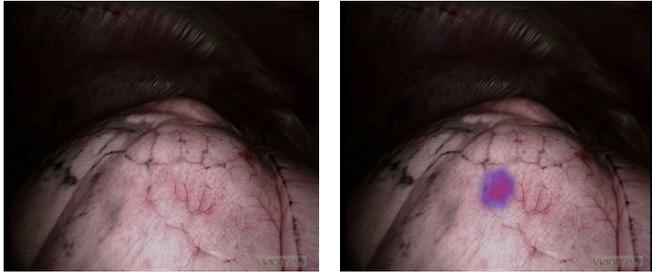
ELUCIDATE TRIAL PRIMARY ENDPOINT: CLINICALLY SIGNIFICANT EVENTS

Clinically Significant Event (CSE)—Instance when cancer was detected with CYTALUX and not detected under current standards of white light and palpation

Primary Endpoint	n/N	Percent of Patients
Total patients with one or more CSE	53/100	53% (95% CI [43.7, 64.0]; p <0.0001)
Total Number of CSEs	65	
Localization of the primary lung nodule	19/100	19%
Identification of occult synchronous lesion	8/100	8%
Identification of a positive or close margin (≤ 10 mm)	38/100	38%

ELUCIDATE TRIAL: CLINICALLY SIGNIFICANT EVENTS

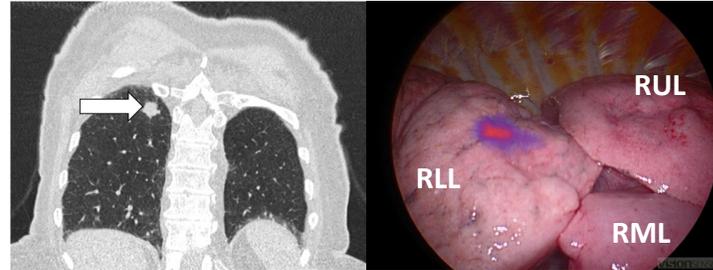
PRIMARY LESIONS



Size of lesions identified by CYTALUX® only	Median	Minimum
Primary lesions	13mm	5mm
Synchronous lesions	8mm	1.5mm

Depth of lesions detected by CYTALUX®	Median	Maximum
CYTALUX® only	10.1mm	27.9mm
CYTALUX® and white light	2.3mm	37.7mm

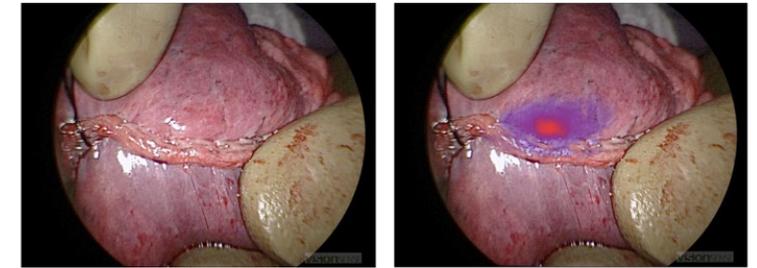
SYNCHRONOUS LESIONS



CAT scan shows no evidence of disease in right lower lobe of the lung

- 8 subjects with additional adenocarcinomas diagnosed with the use of CYTALUX®
- Majority of additional cancers were outside the planned resection field

CLOSE RESECTION MARGINS



Margin Distance	Number	Percent
≤5mm	23	60.5%
>5mm – 10mm	15	39.5%

Margin CSE Concordance with Pathology	Number	Percent
Close resection margins measured ≤10mm by pathology	32 [†] /36*	88.9%

*Two IMI Positive Margins did not report margins by pathology
 †Two were measured 11mm and two were >11mm by pathology

Surgeons indicated a change in scope of their procedures in **29%** of patients

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