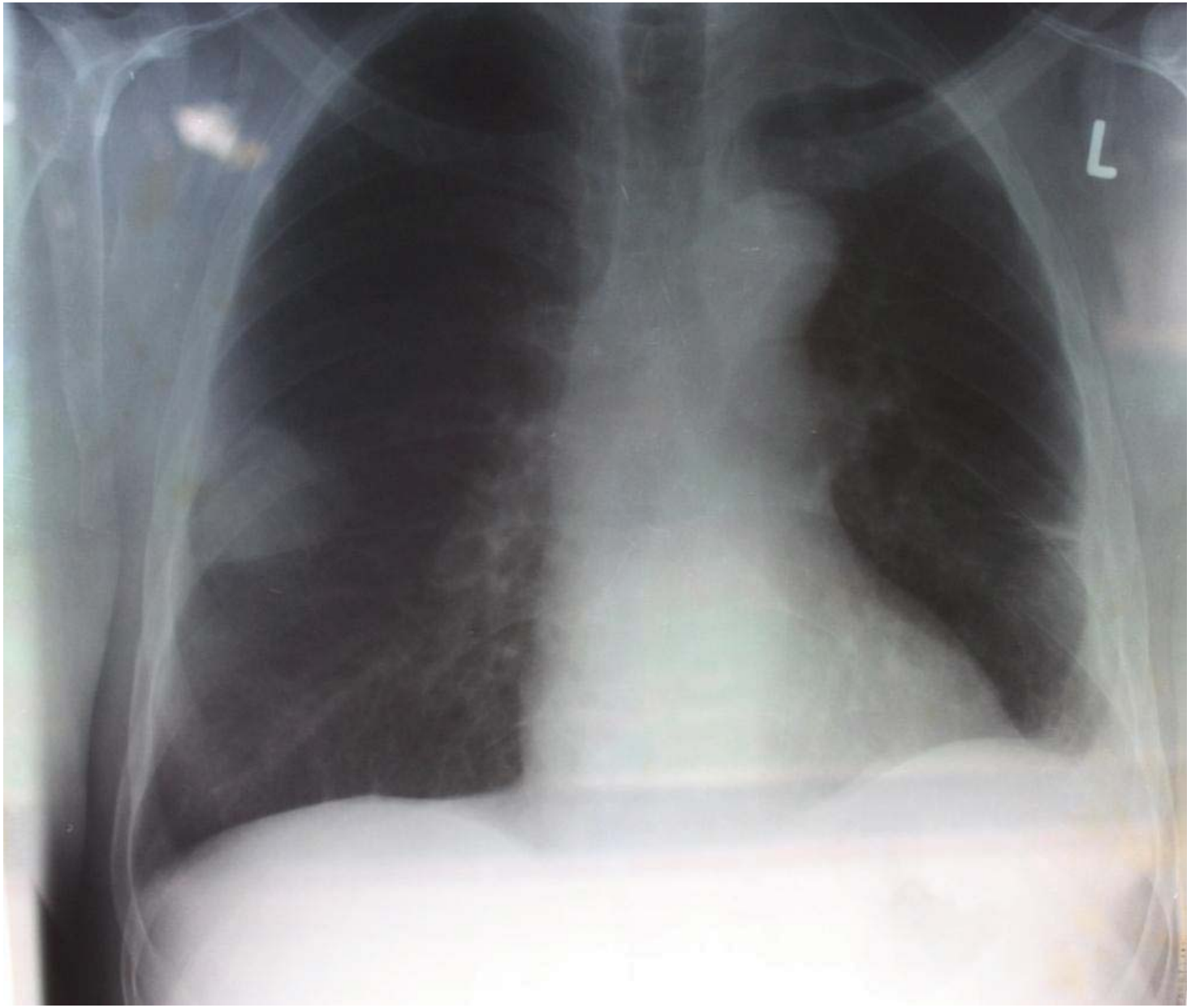
58yoM with lung mass

- Cough for ~12 months
  - Morning through night
  - Non-productive
  - SOB while working
- Smoker (35yrs, 1 box/day over past year)
- Heavy alcohol use
- HIV negative 7/2011

58yoM with lung mass

March 2011

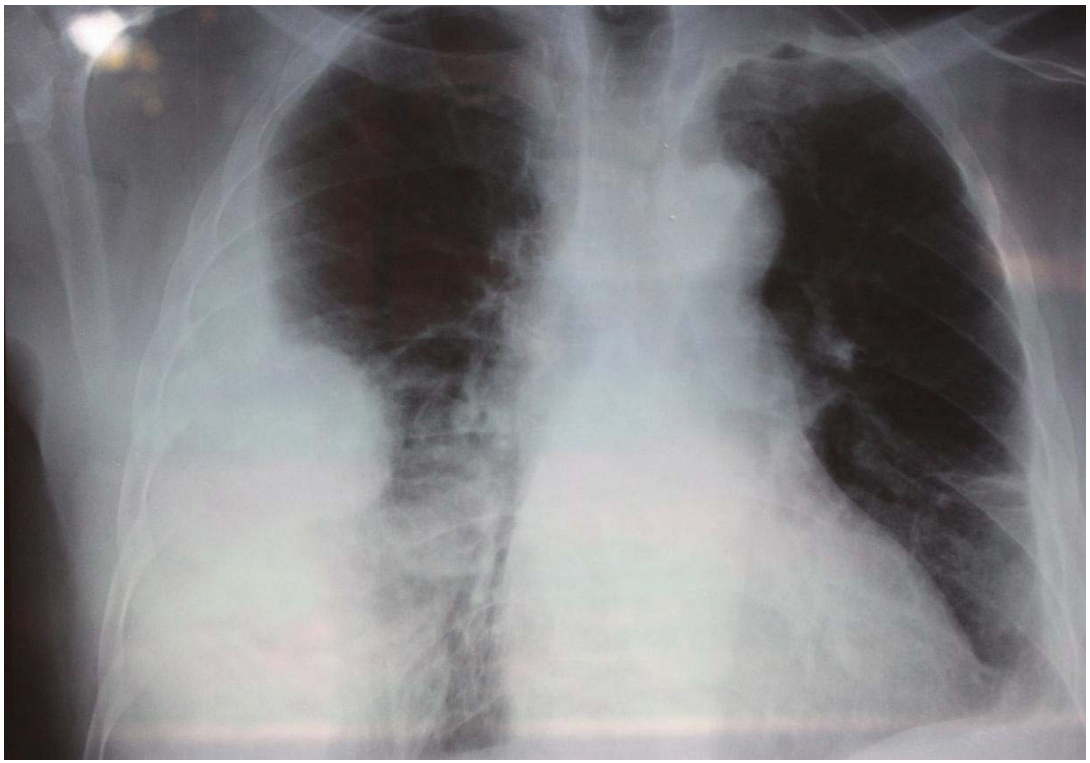


58yoM with lung mass

- May 2011
  - Cough, slight chest pain
  - Saw private doctor

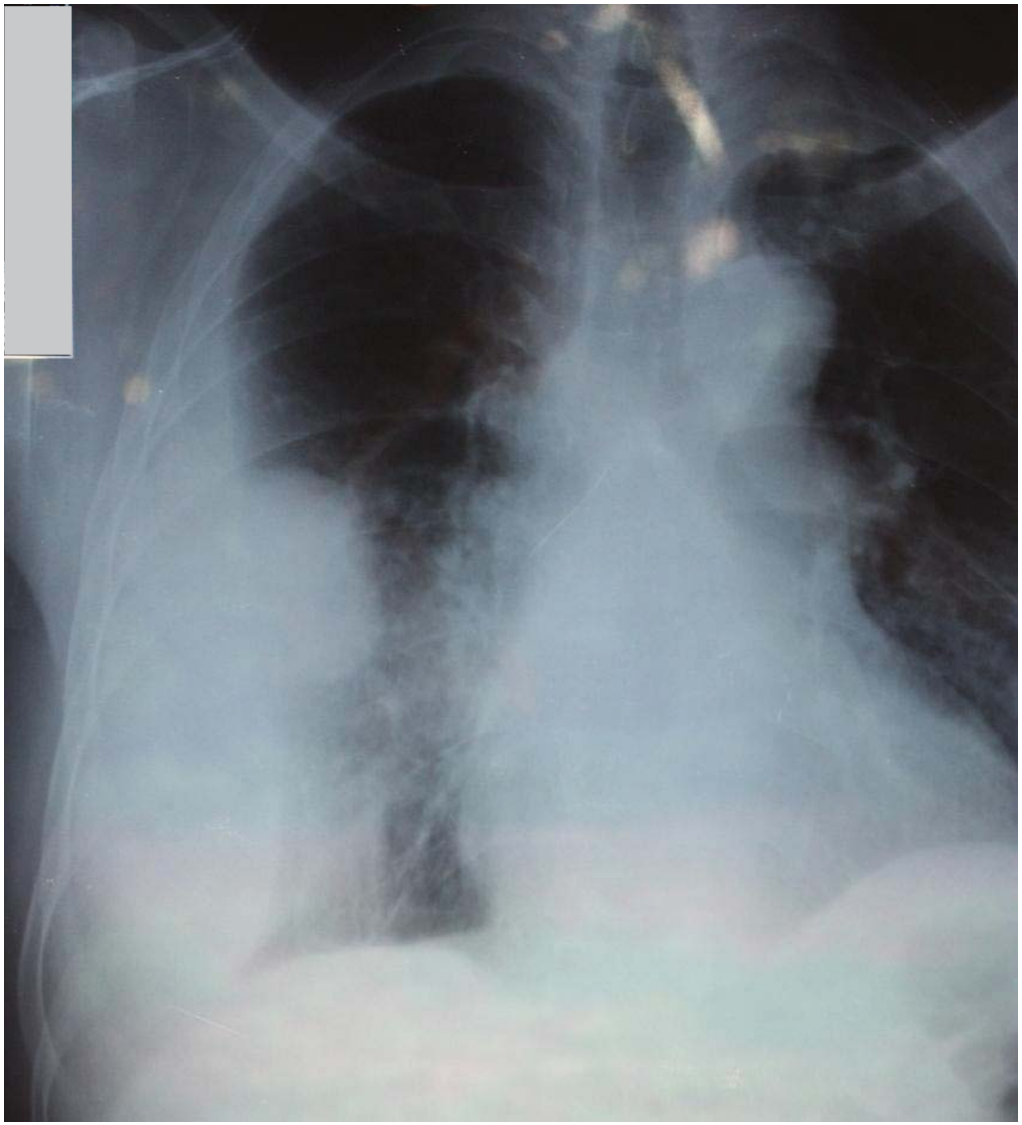
58yoM with lung mass

- Presented to A&E at PMH



PA CXR 9/2011

58yoM with lung mass



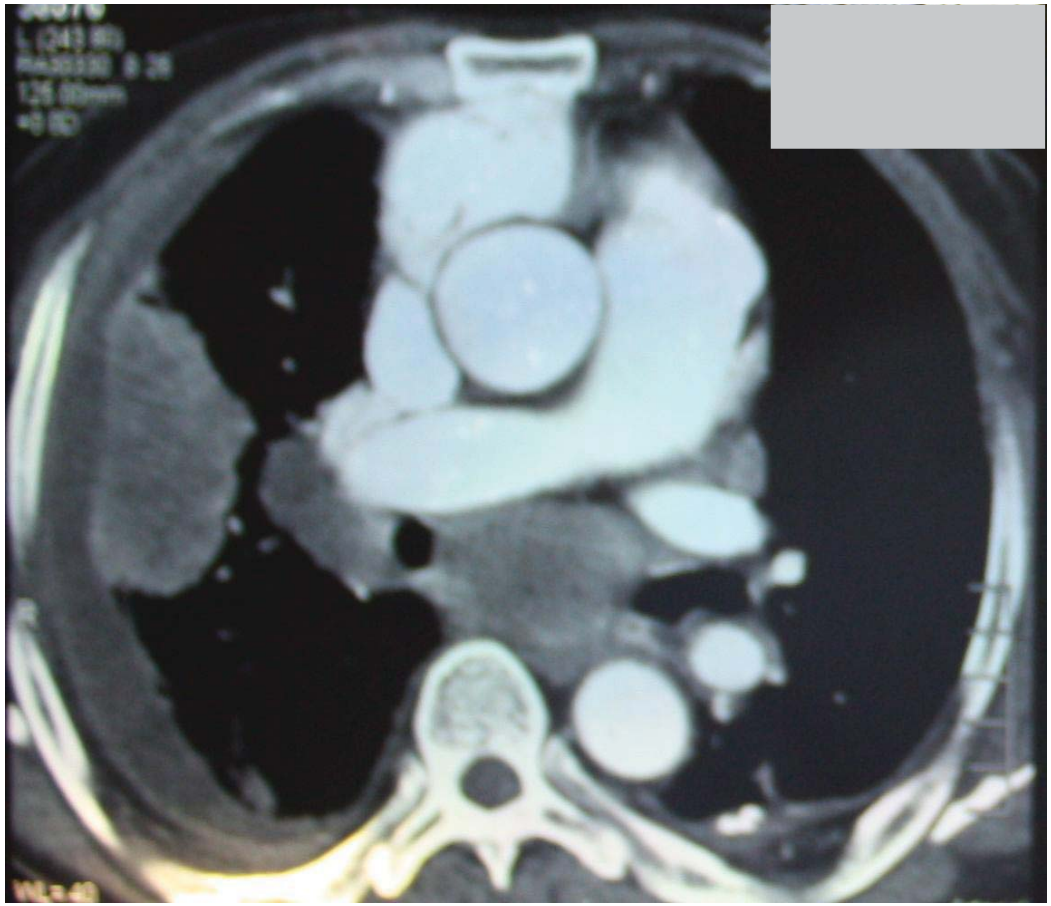
PA CXR 10/2011

58yoM with lung mass

- Diagnostic thoracentesis
  - Cell counts/chemistries not available
  - Cytology 9/2011):
    - Brownish fluid, 4.5ml
    - Pleural fluid shows innumerable mature small lymphocytes (lymphocytosis). Negative for malignant cells. The lymphocytosis is suggestive of tuberculosis.
- Started anti-TB therapy

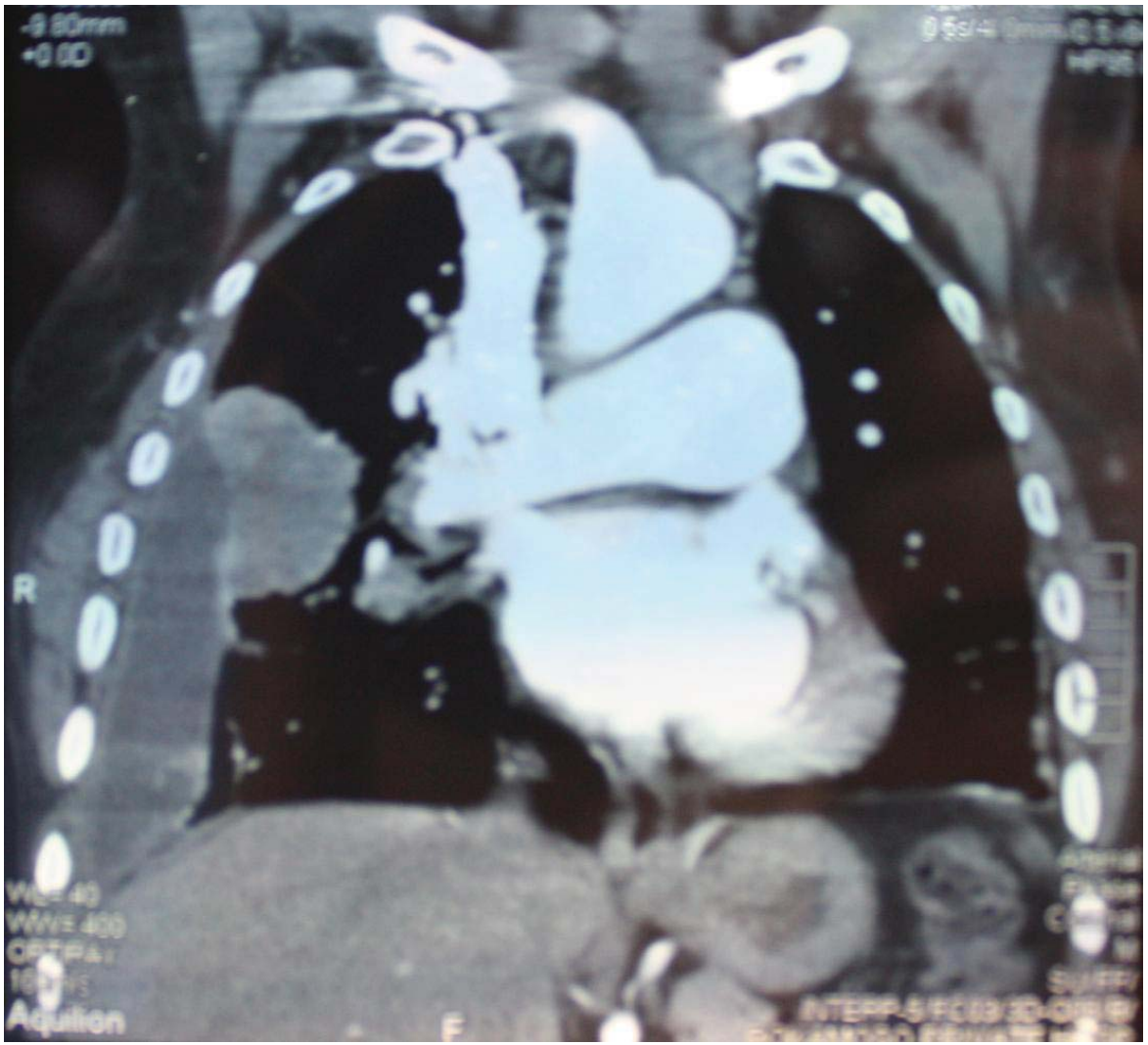
58yoM with lung mass

- Referred to Bokamoso Private Hospital for CT, PMH CT scanner not working
  - Non-contrast chest CT November 2011



58yoM with lung mass

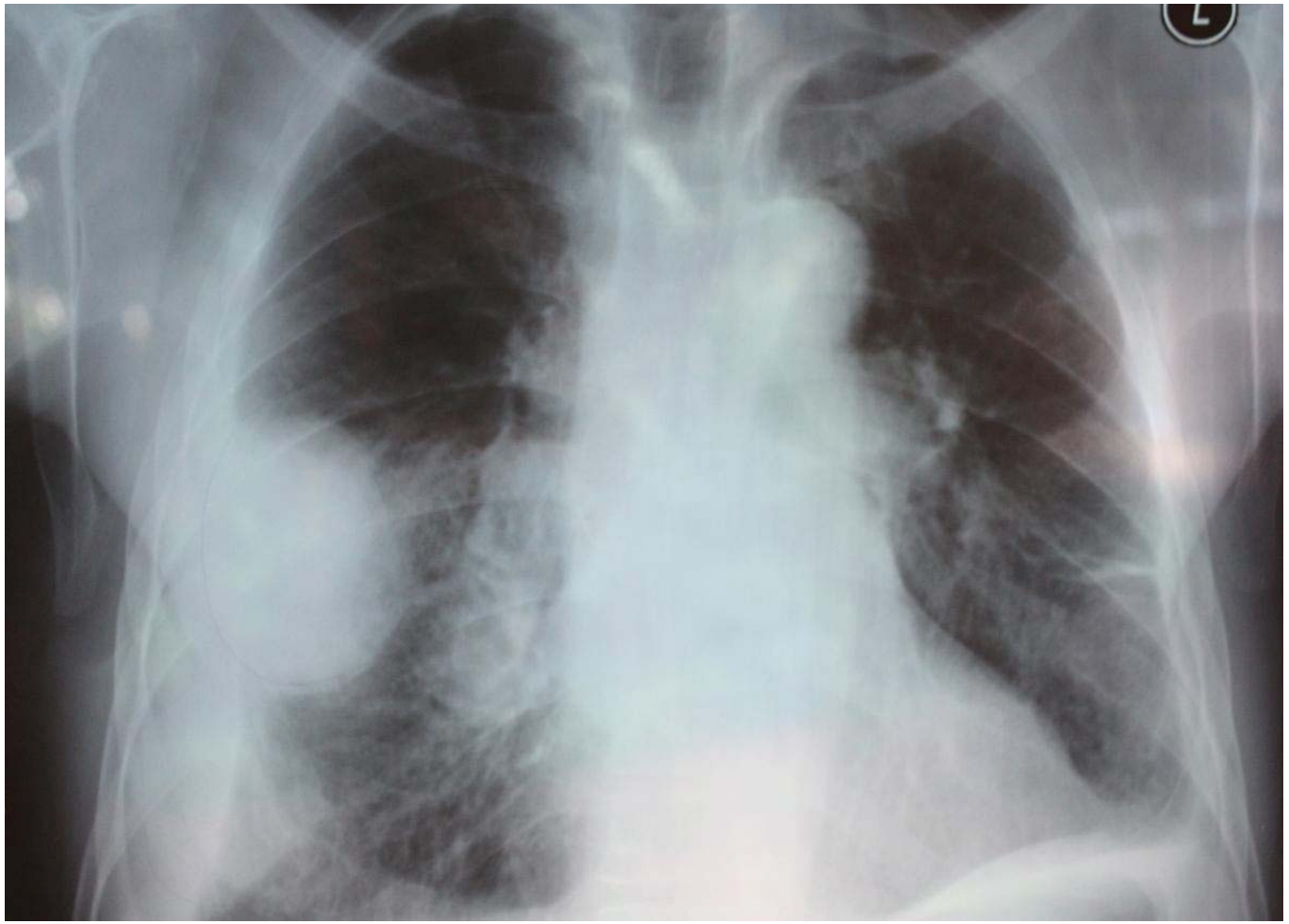
– Non-contrast chest CT November 2011

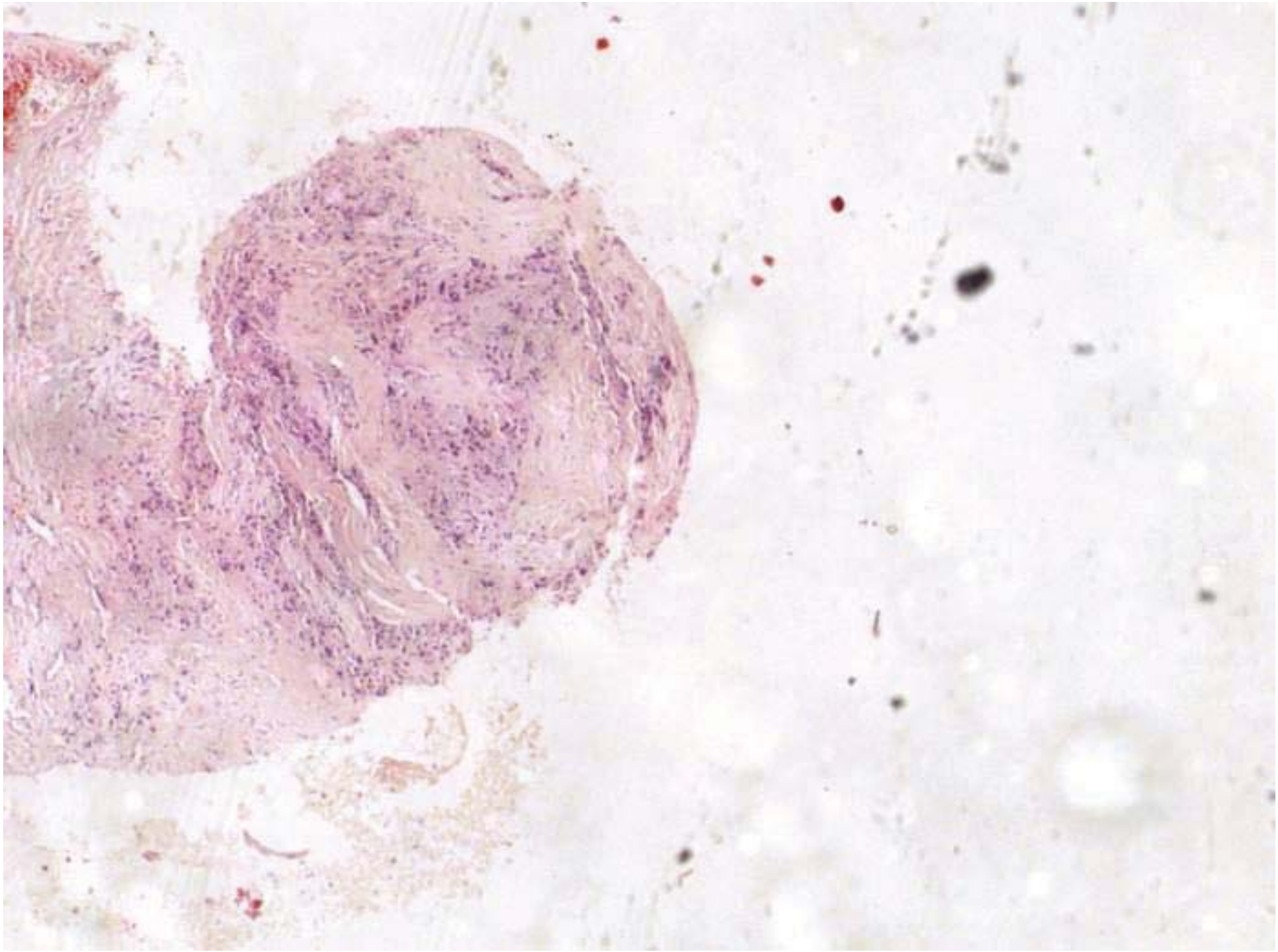


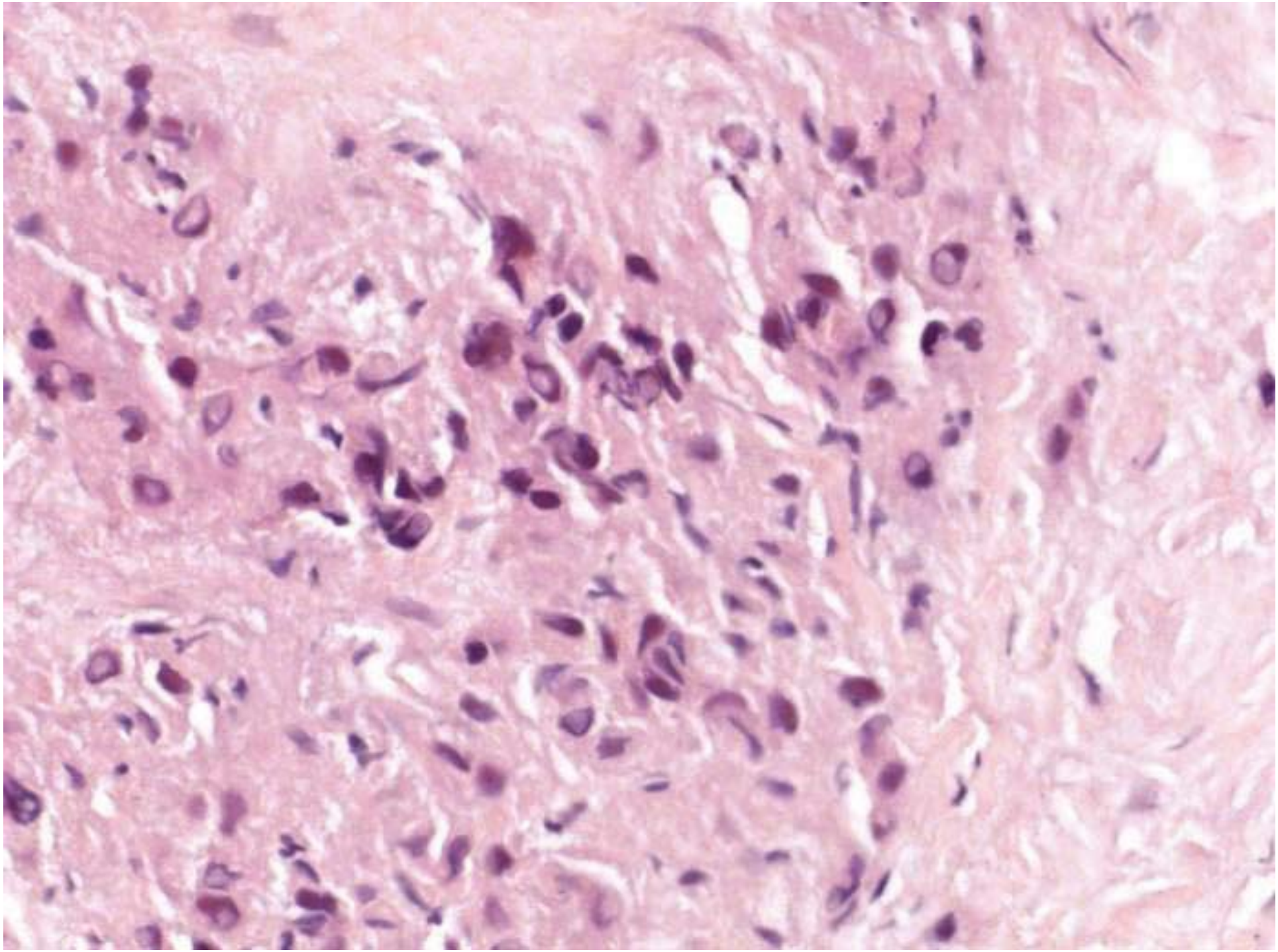
58yoM with lung mass

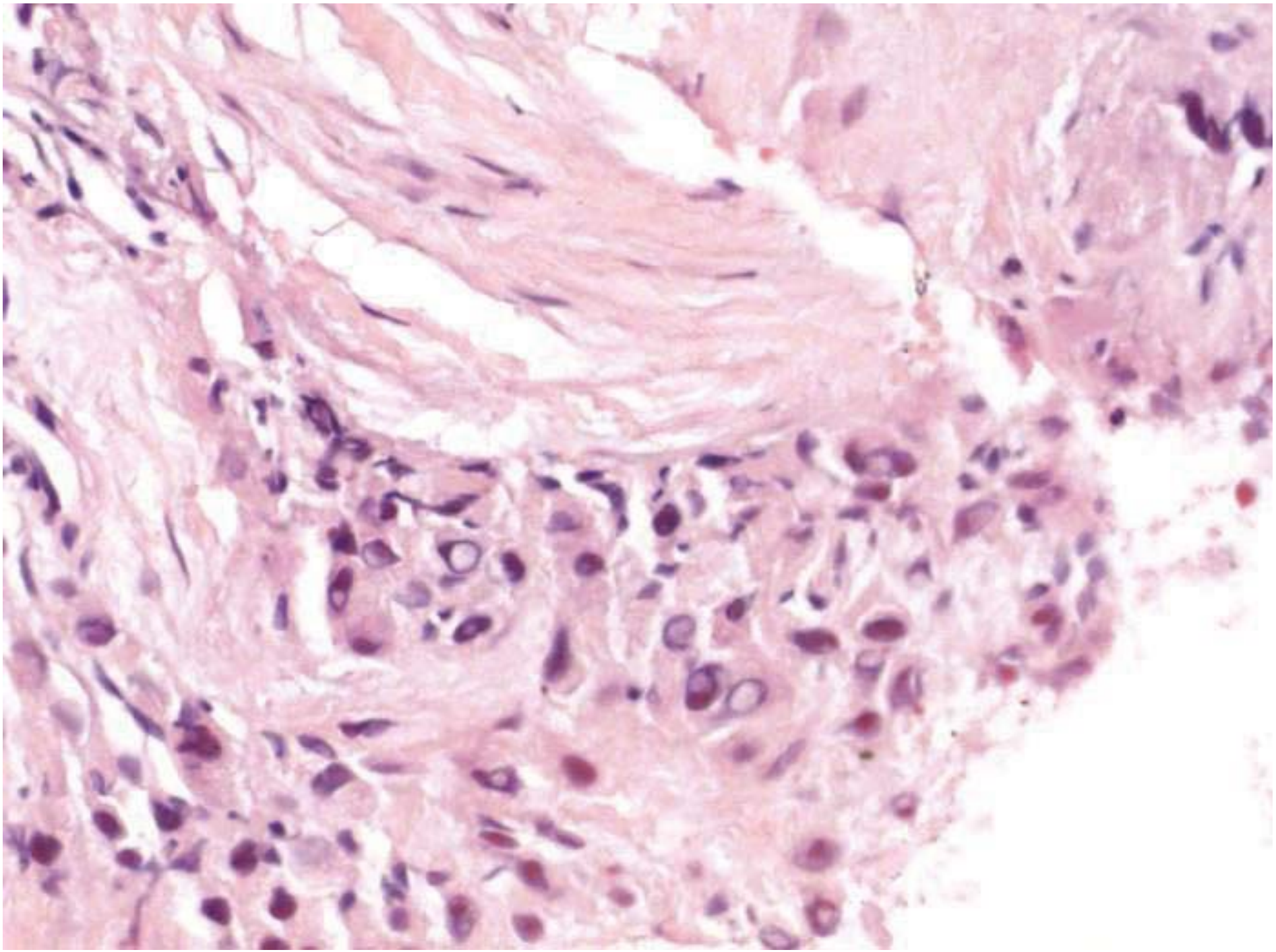
- Ultrasound guided FNA (1/2012)

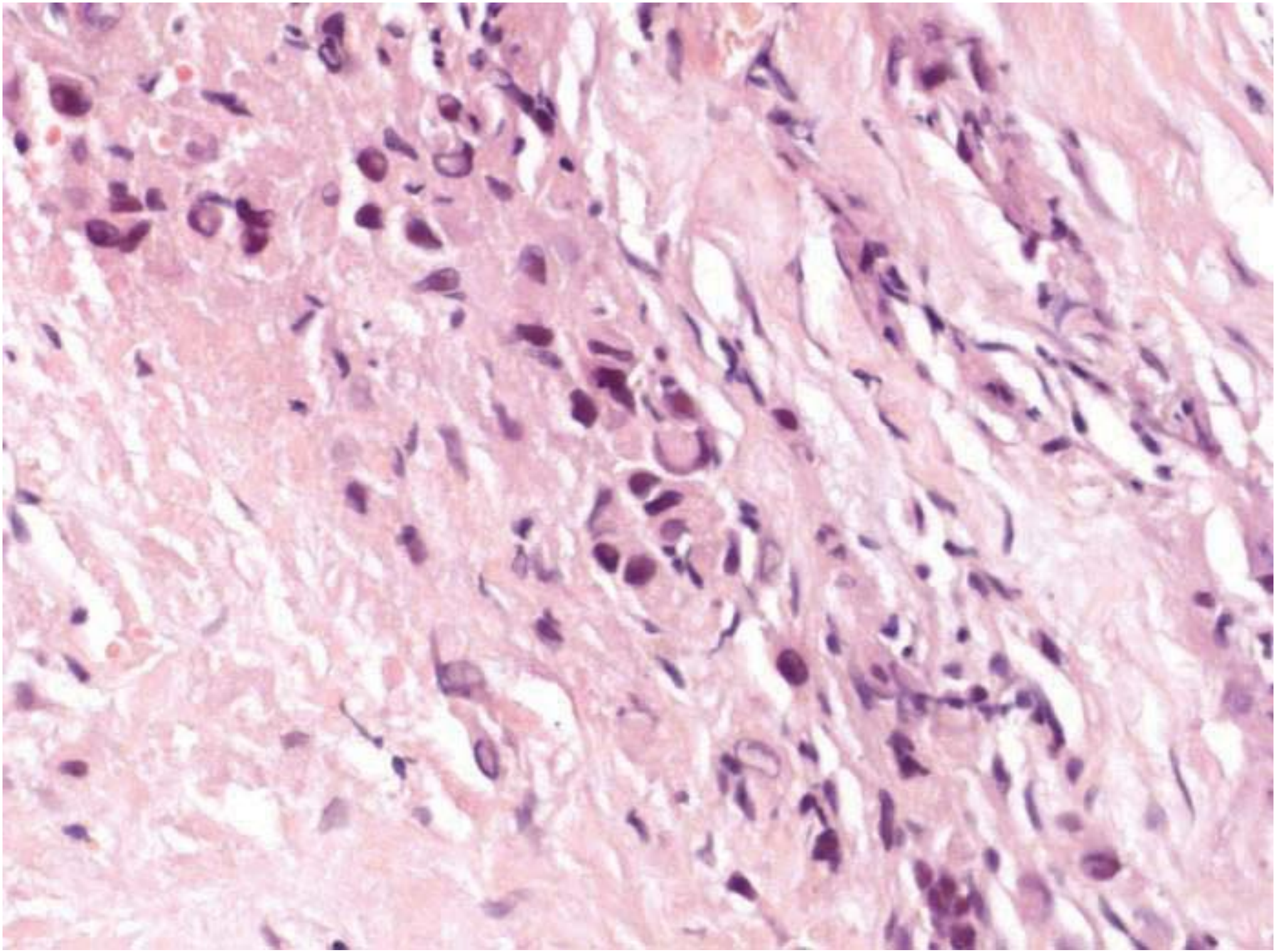
January 2012

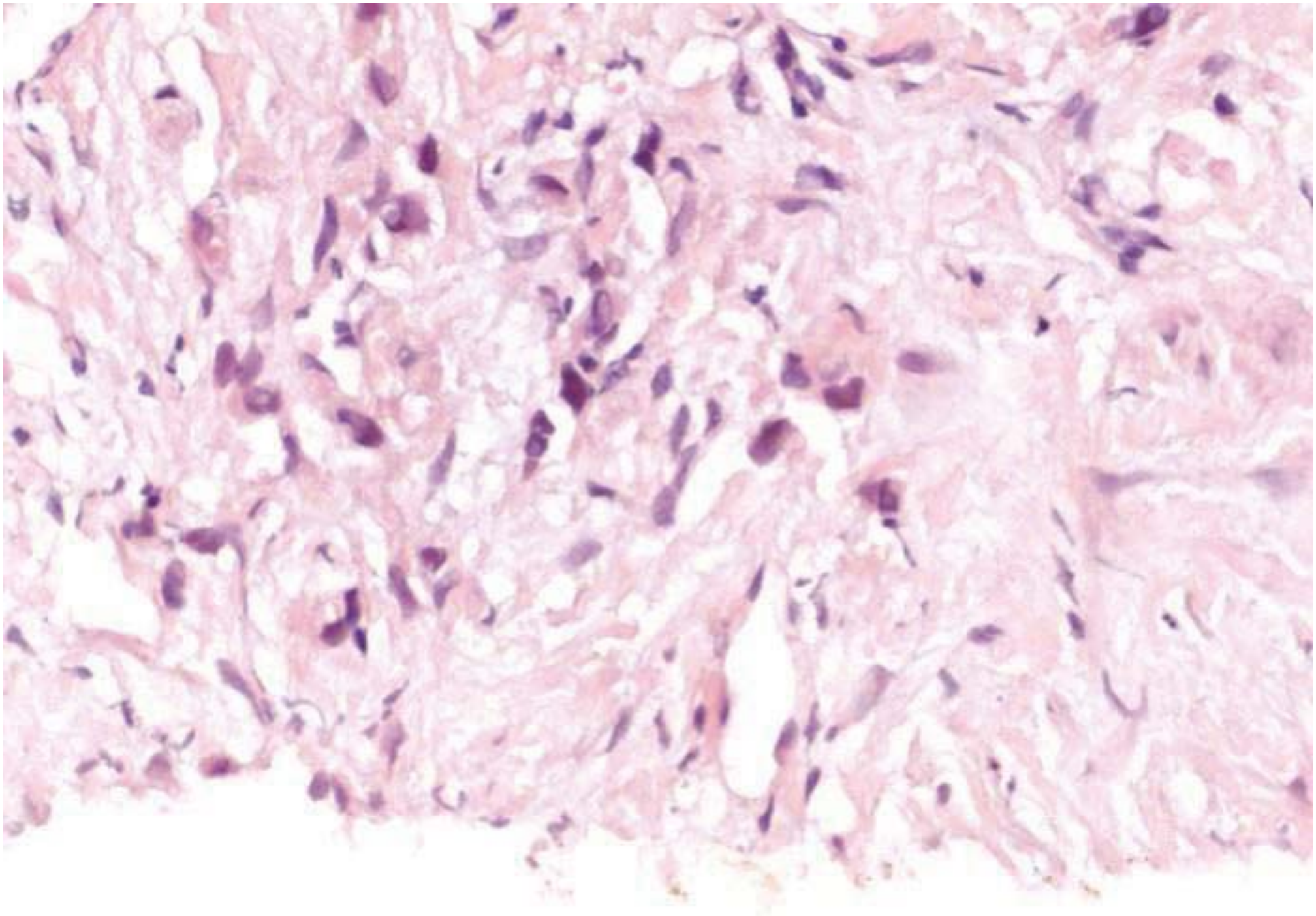


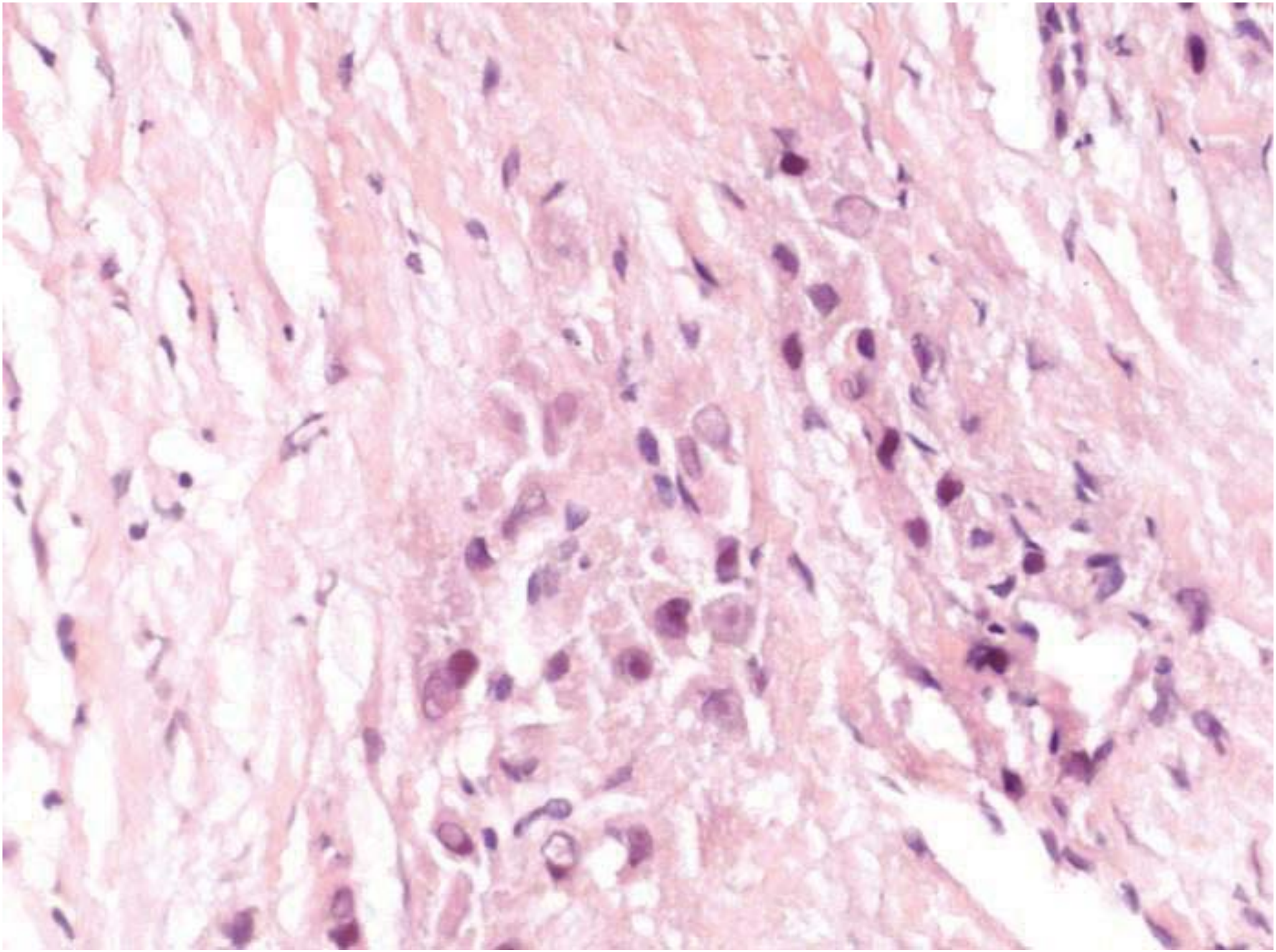


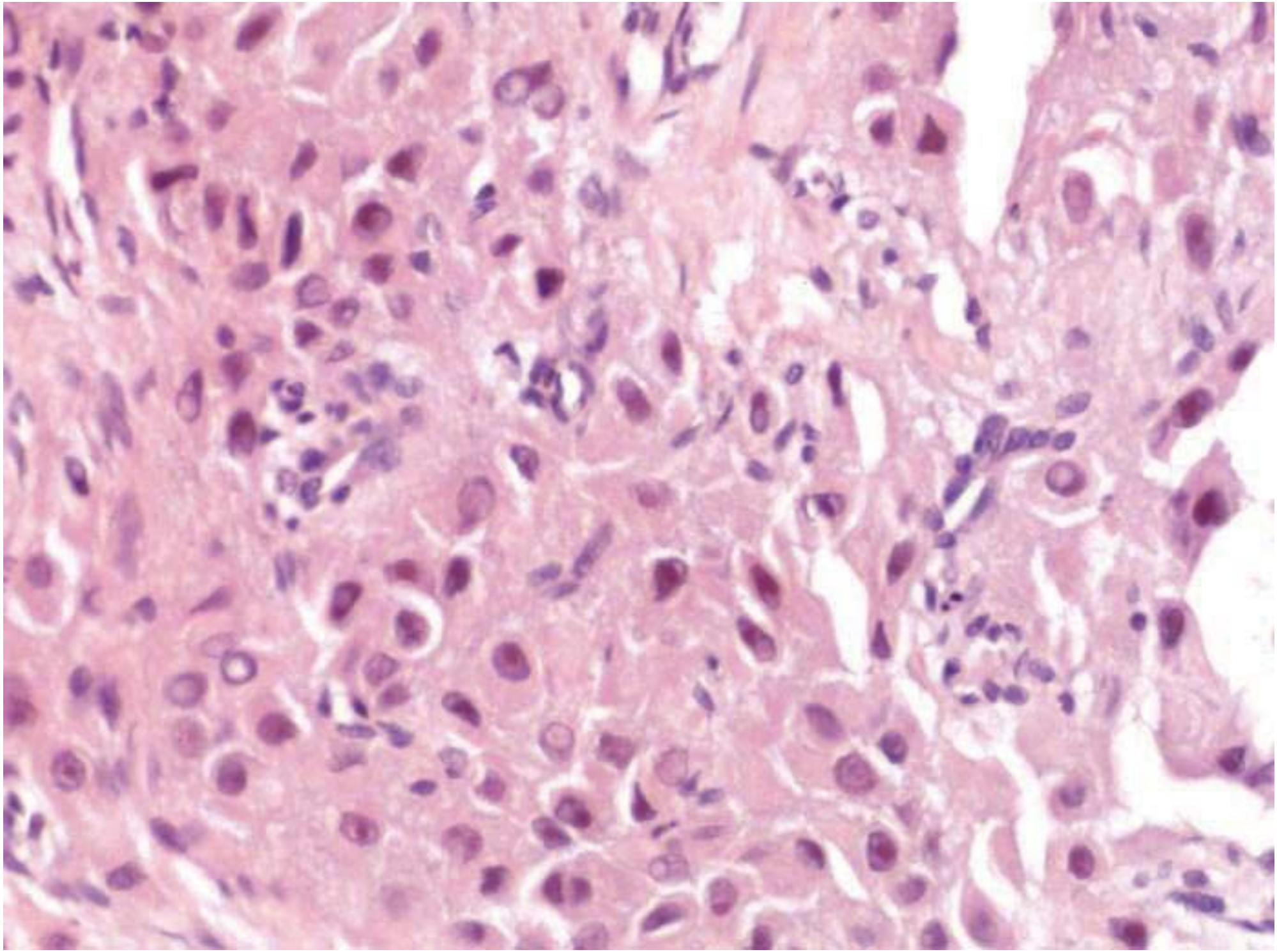


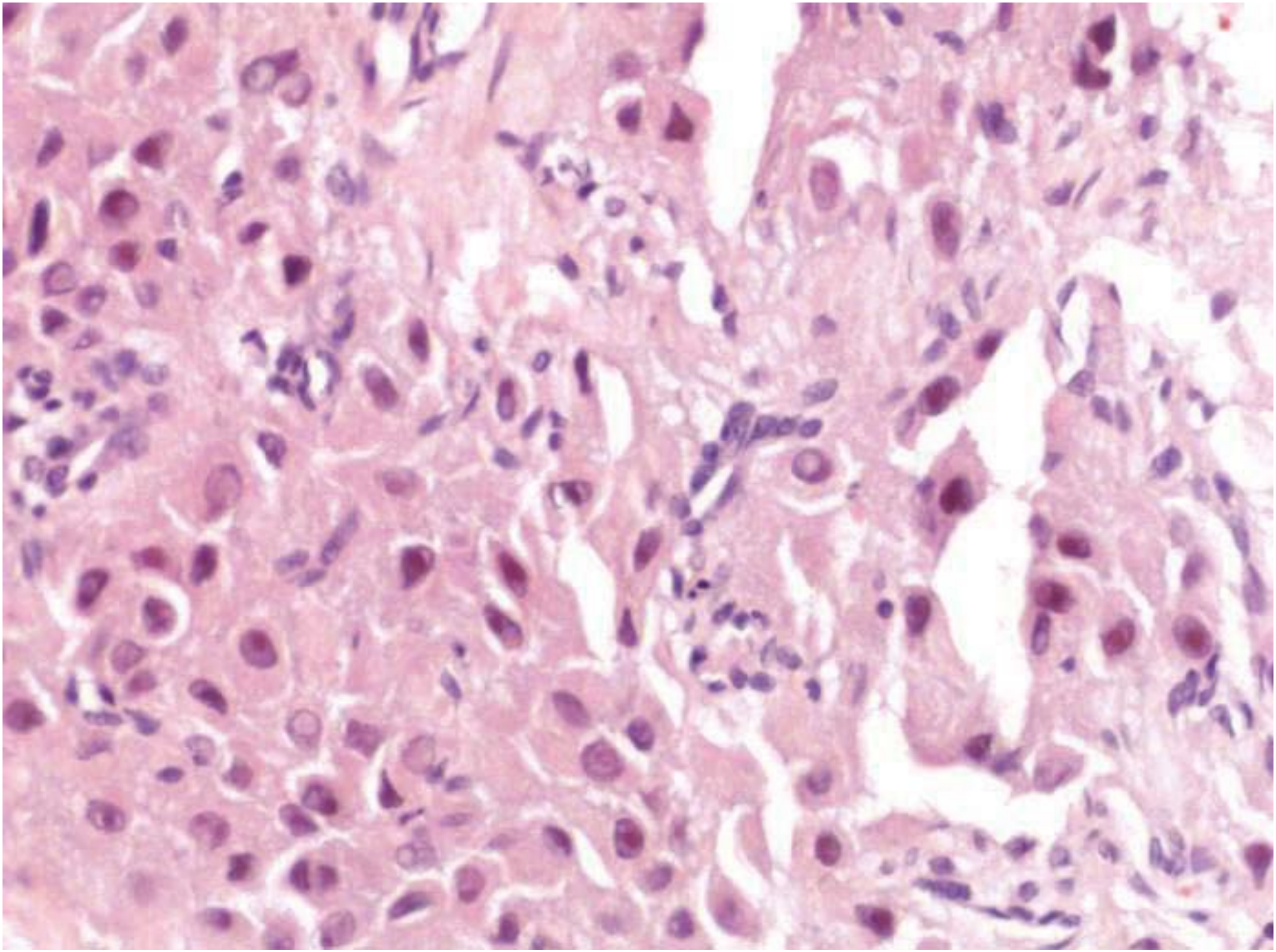


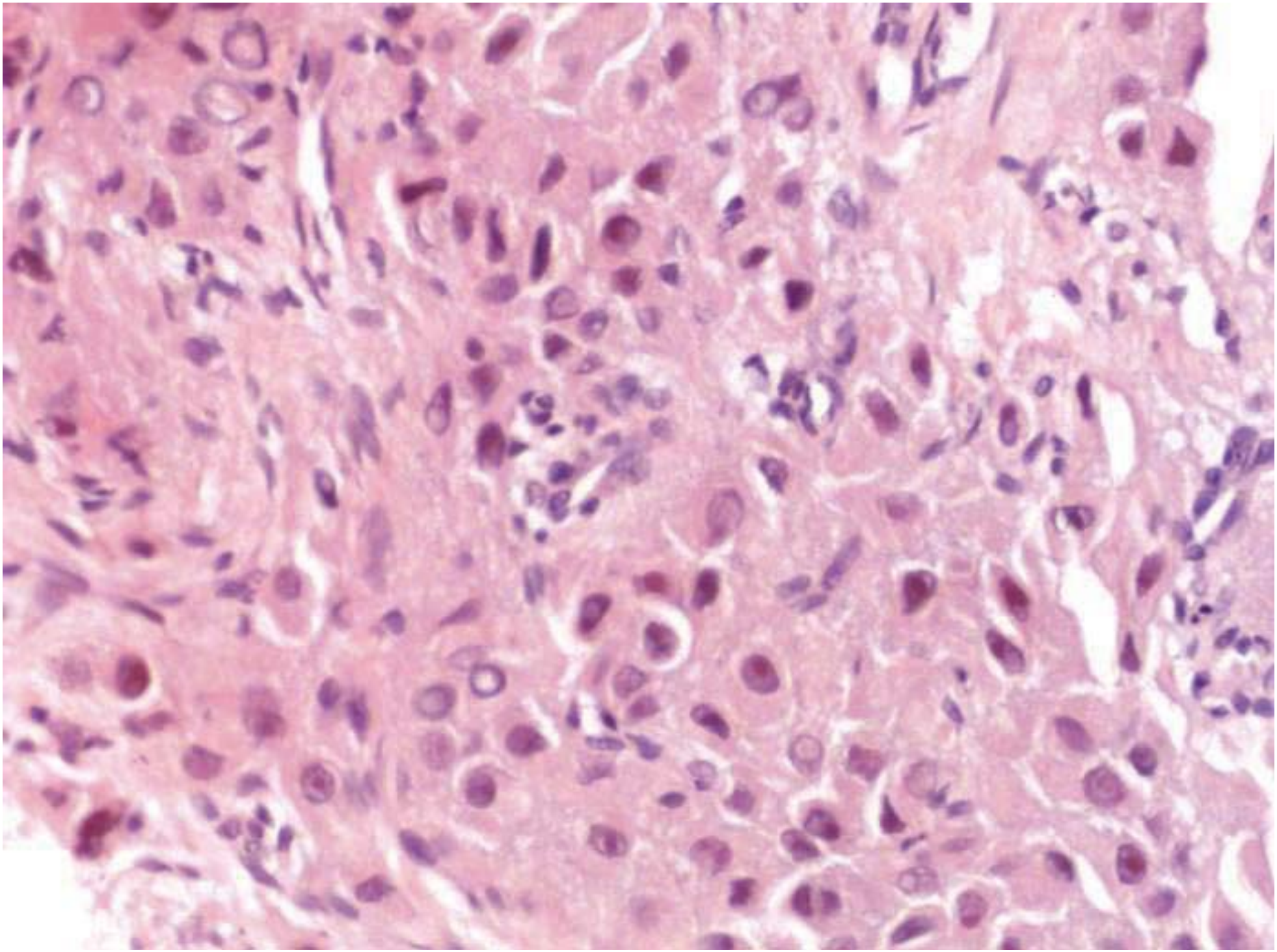


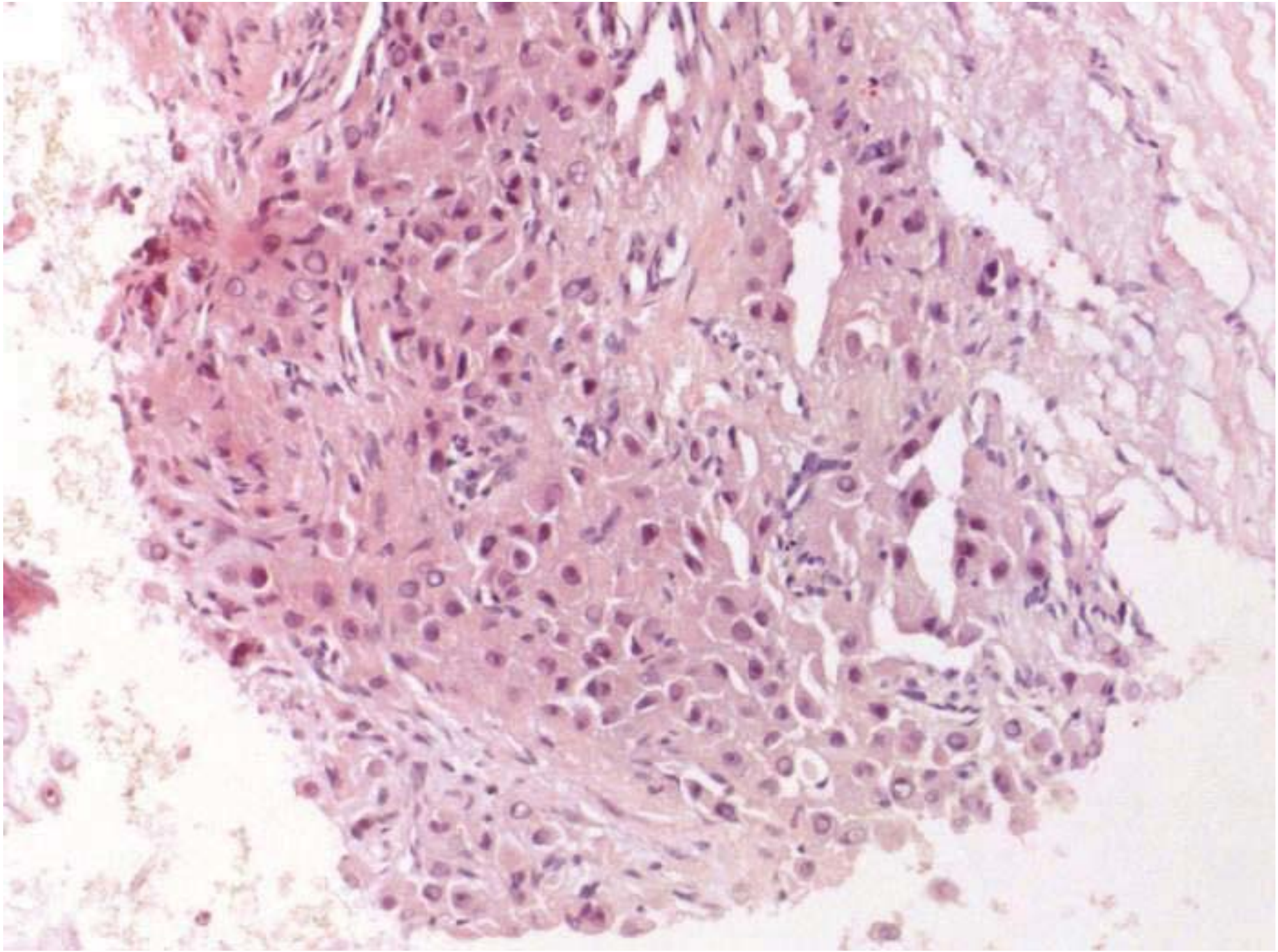


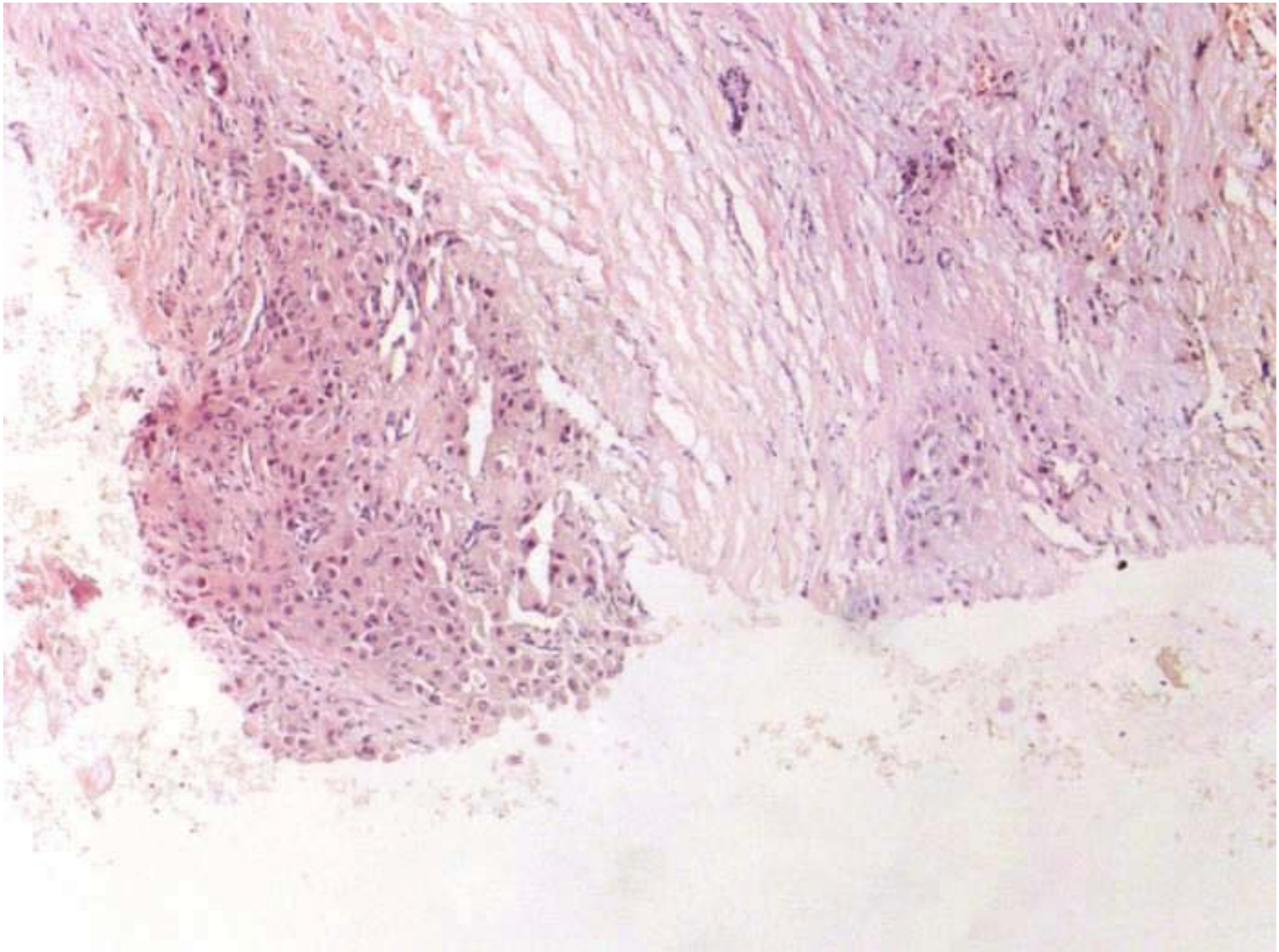


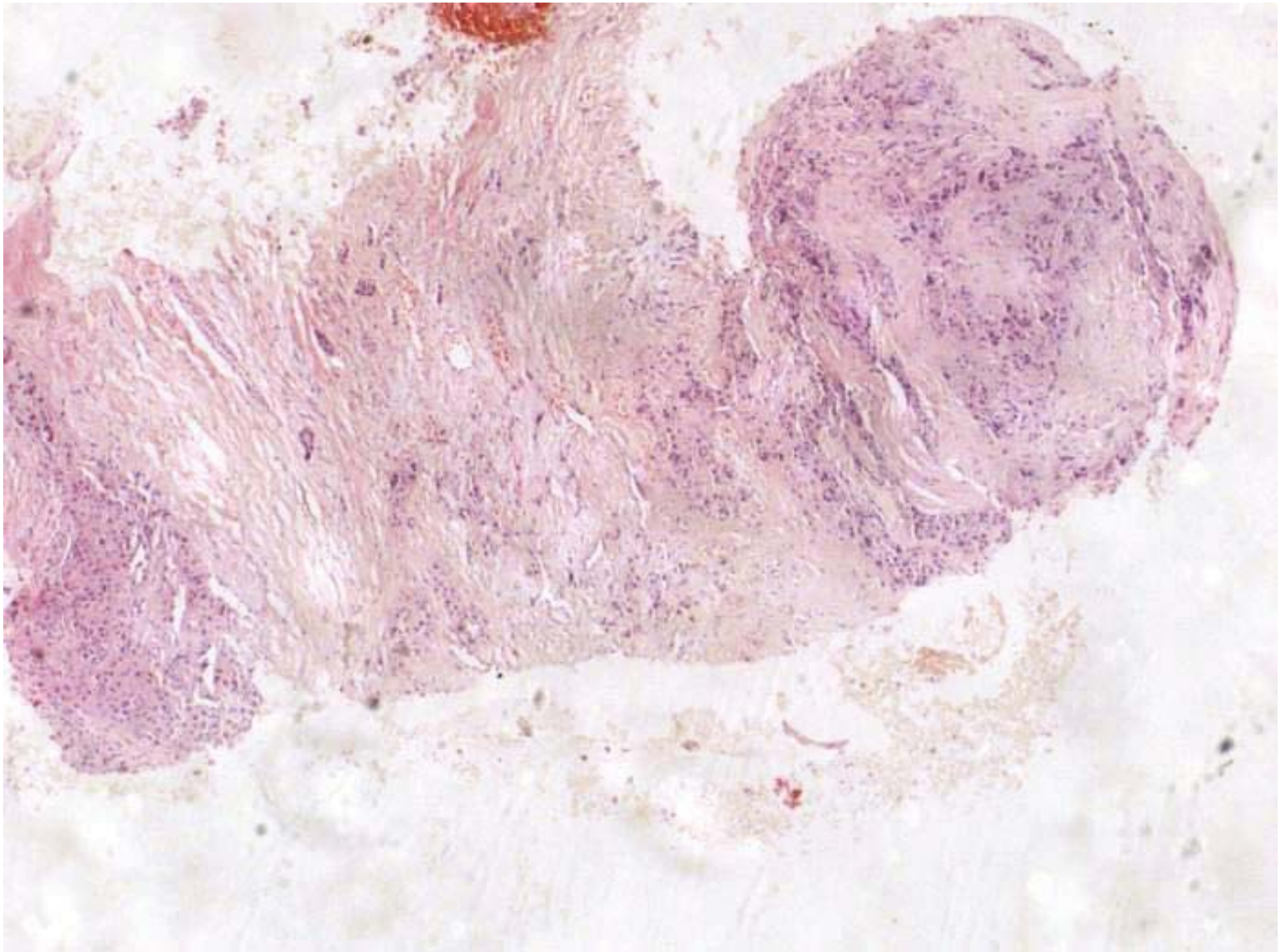












58yoM with lung mass

- Microscopy: Smear shows numerous poorly differentiated anaplastic epithelial cells. Some of them are forming glandular structures.
- Diagnosis: Poorly differentiated adenocarcinoma (?metastatic)

58yoM with lung mass

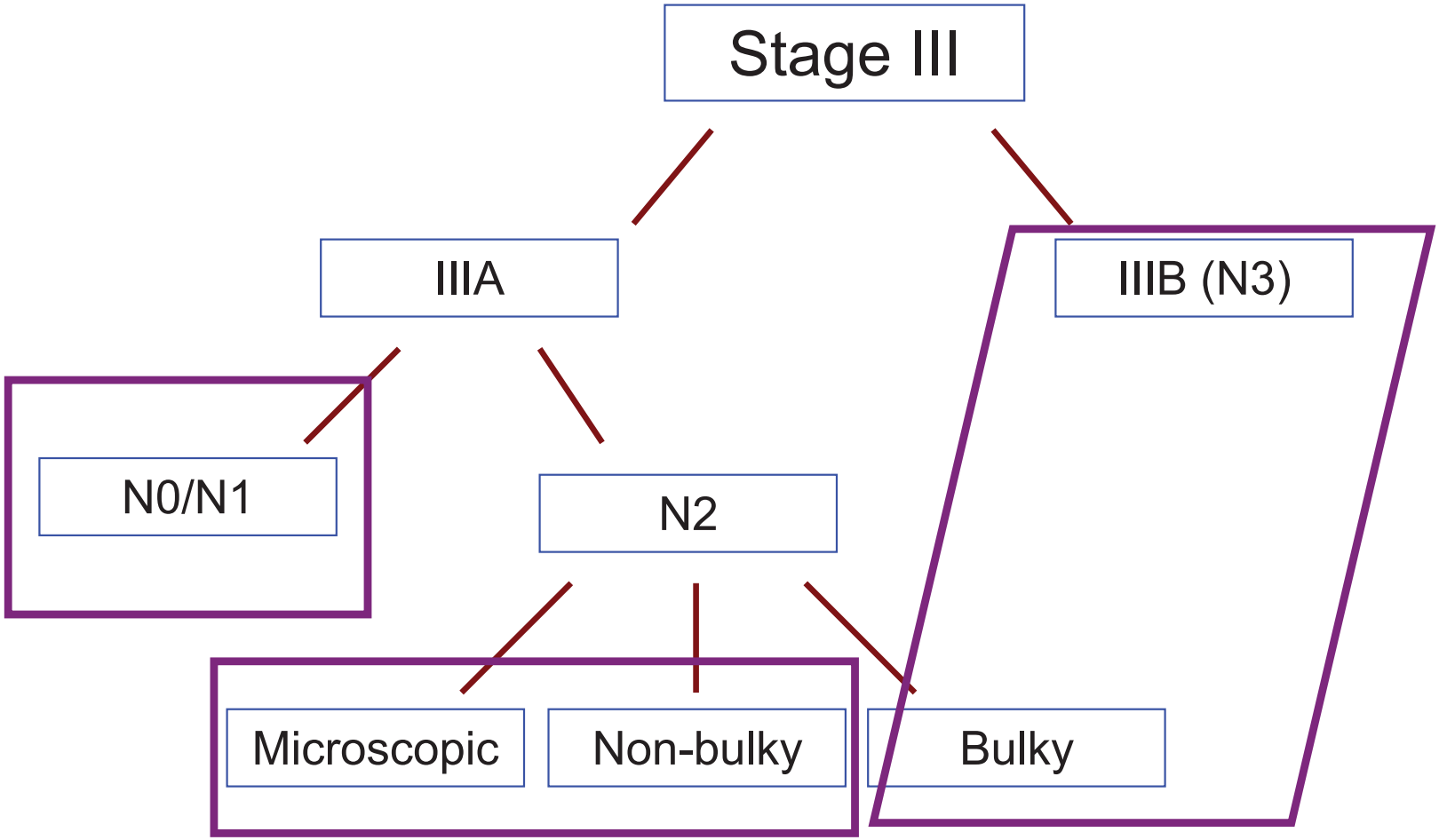
- Exam:
  - Appears well and cognitively intact
  - No lymphadenopathy
  - No abdominal mass
  - Lungs clear

Locally Advanced Lung Cancer

Benjamin Falit, MD
Kerry Massman, MD
Botswana Multidisciplinary Tumor Board
April 17, 2012

Potentially Resectable Disease:

Surgical Candidate or No?

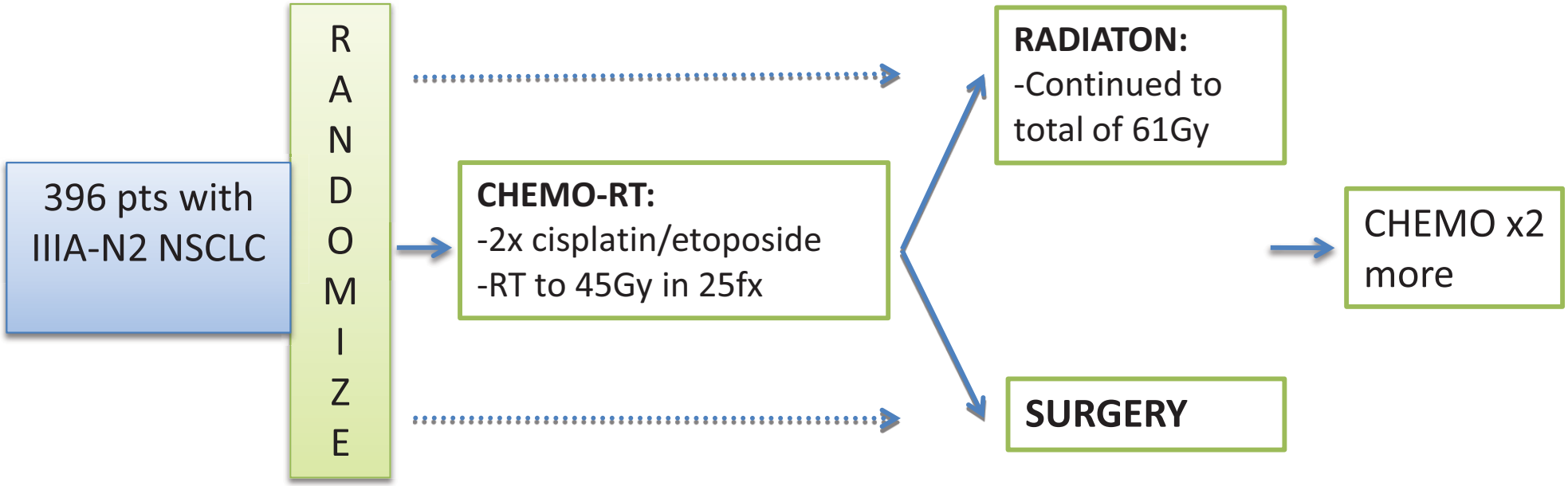


Also to consider:

- Overall health of patient
- Operable vs inoperable

*Bulky = >2cm, multi-station, ENE

INT 0139: Surgery vs definitive chemoRT



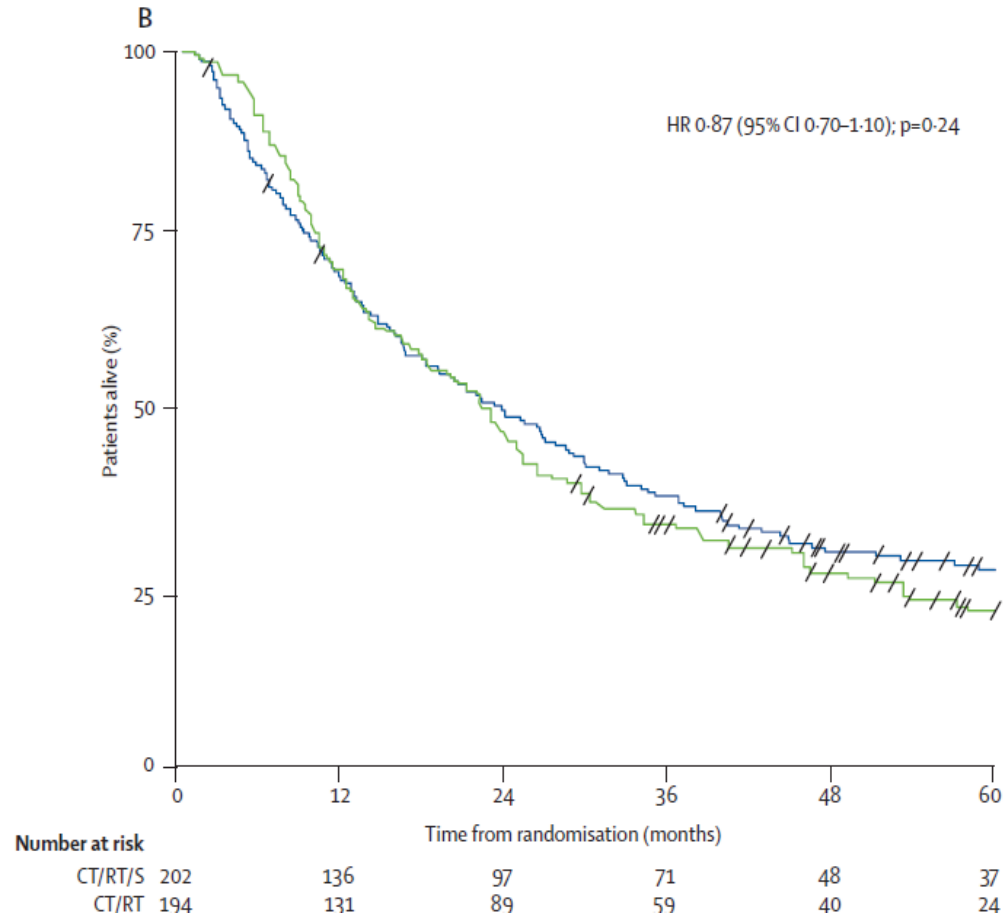
Eligibility:

- IIIA-N2 (T1-T3) NSCLC
- Histologically confirmed N2
  - and confirmed negative any N3 node >1cm
- PS 70-100
  - But if 70-80 needed albumin 85% of nl and <10% wt loss

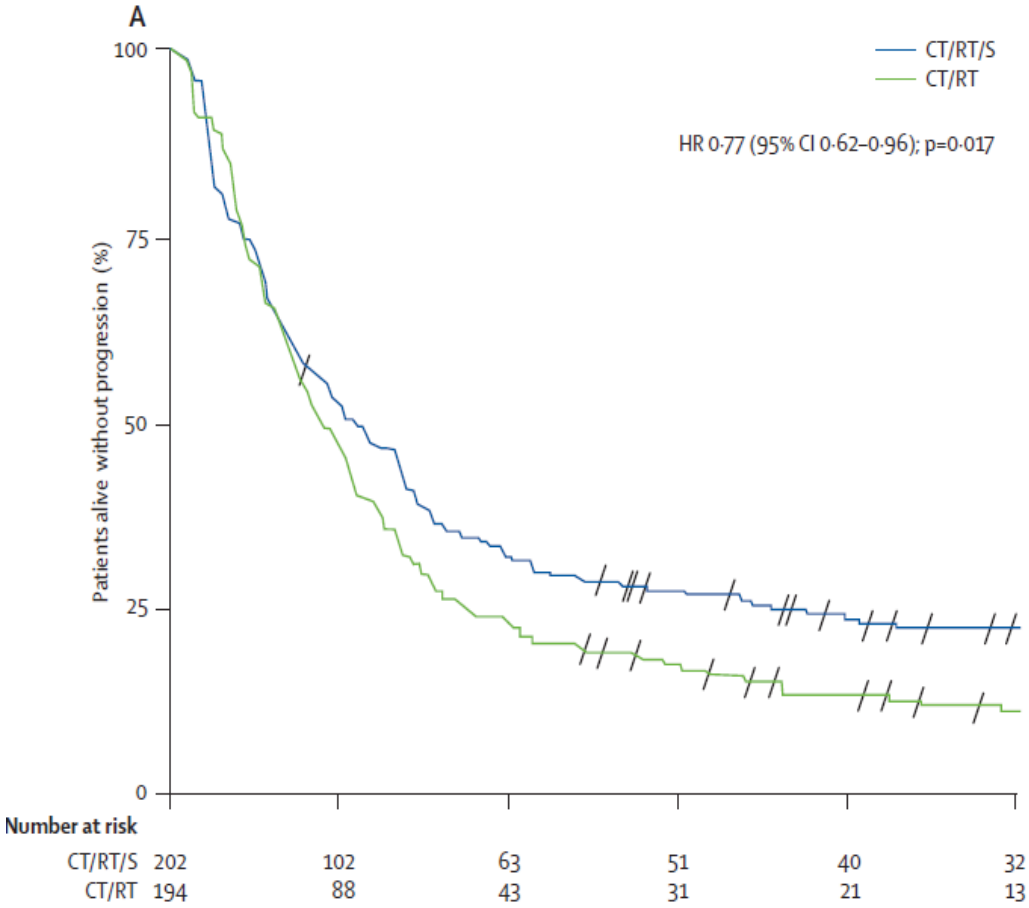
Albain et al, Lancet 2009

INT 0139: Results

OS

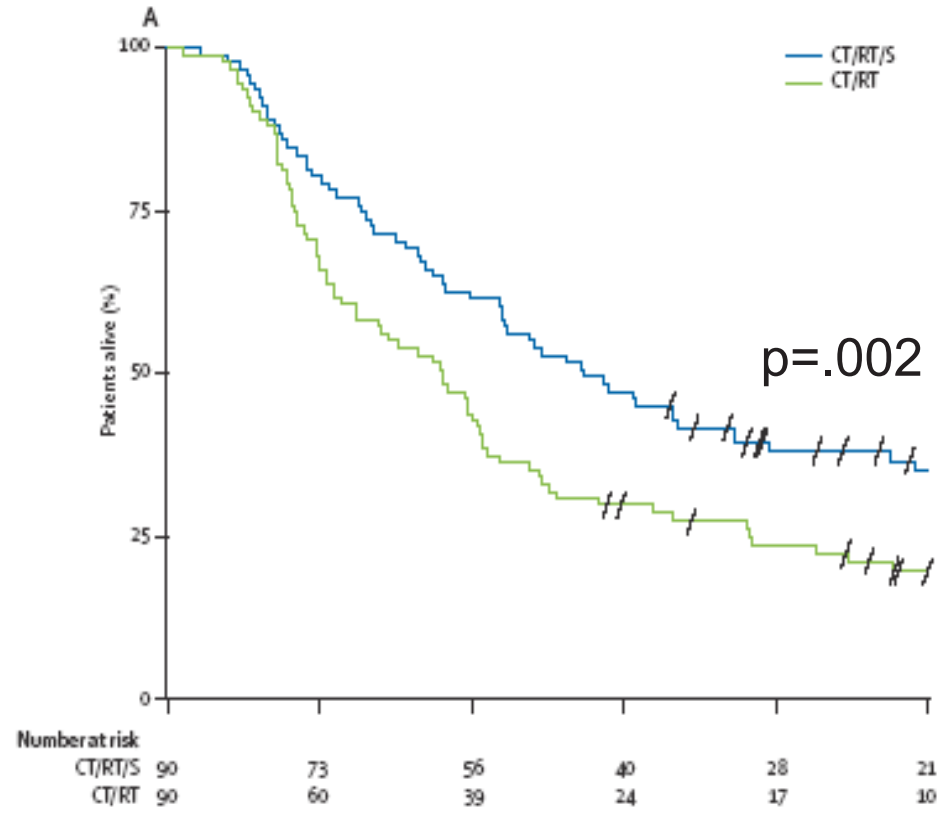


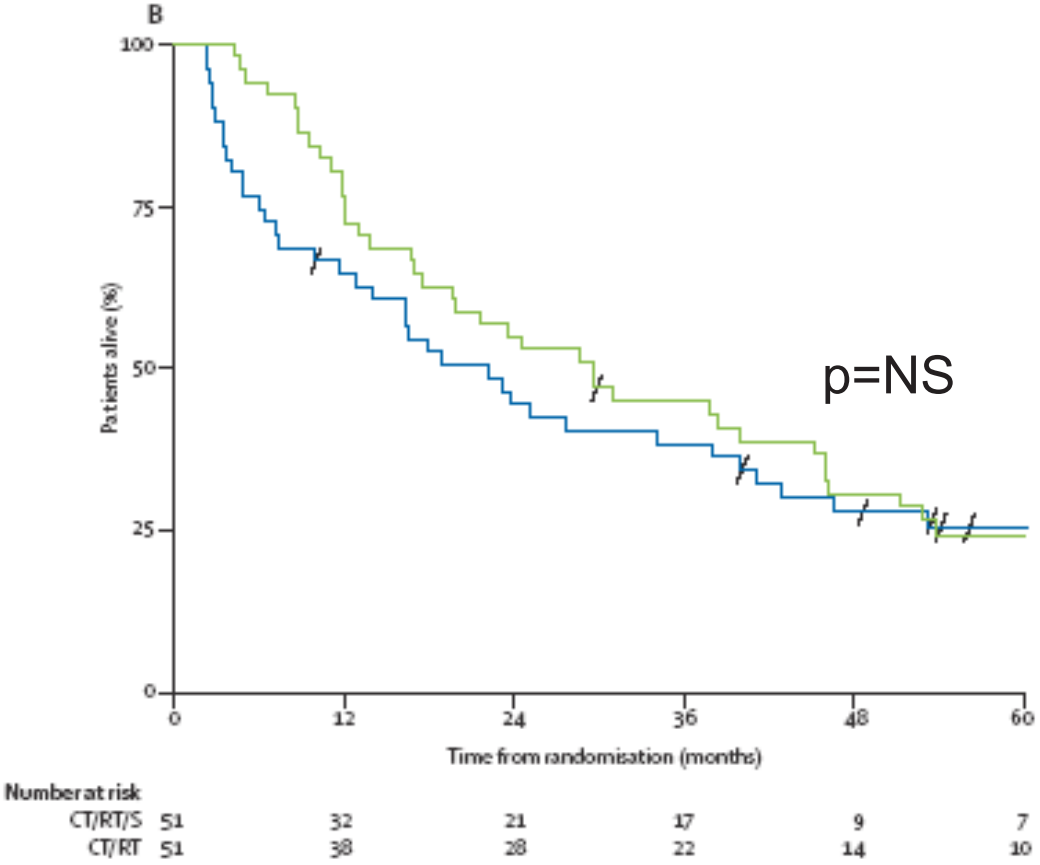
PFS



Albain et al, Lancet 2009

Overall Survival with Lobectomy vs Pneumonectomy





*155 Resections (3 wedge, 98 lobe, 34 pneumo)
*26% Mortality with pneumonectomy

Albain KS, et al, Lancet 2009

INT 0139: Conclusions

- No OS difference between definitive RT and surgery following induction chemoRT
- High rate of peri-operative mortality after pneumonectomy
- Best option may be trimodality therapy if lobectomy can be employed

Albain et al, Lancet 2009

Unresectable Disease: Definitive/Concurrent Chemo/RT

Sequential vs Concurrent Chemoradiation for Stage III Non–Small Cell Lung Cancer: Randomized Phase III Trial RTOG 9410

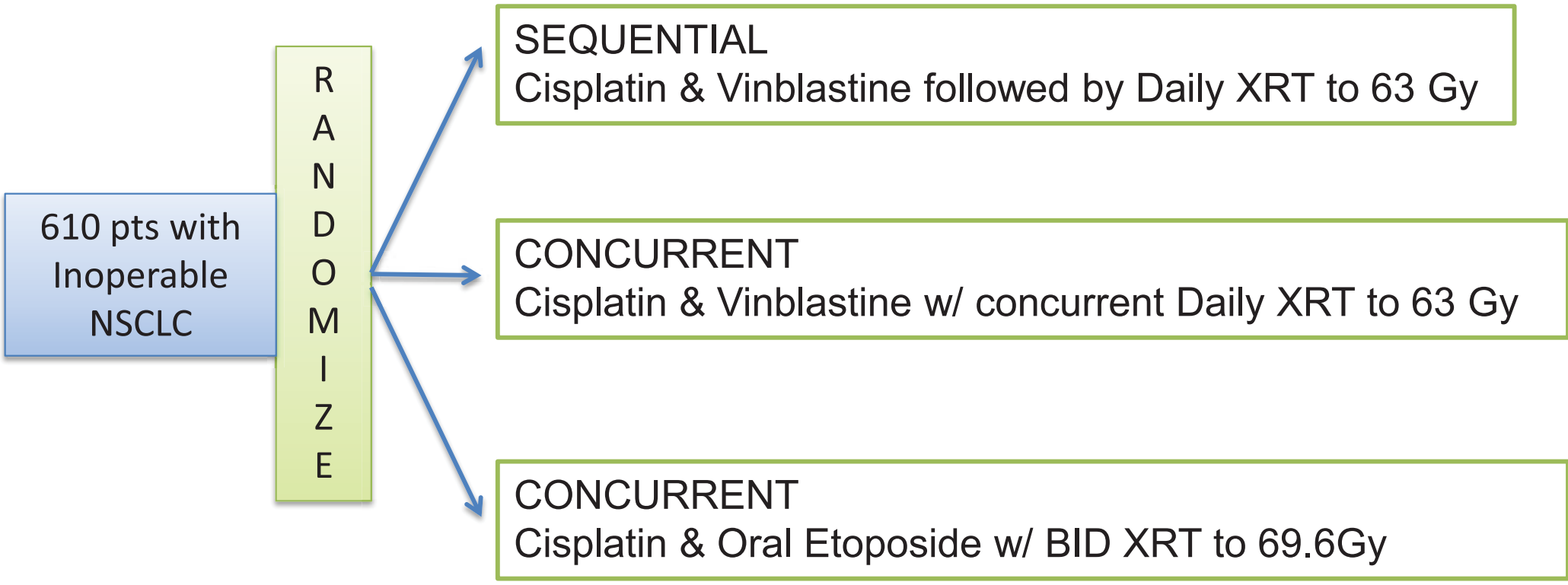
Walter J. Curran Jr, Rebecca Paulus, Corey J. Langer, Ritsuko Komaki, Jin S. Lee, Stephen Hauser, Benjamin Movsas, Todd Wasserman, Seth A. Rosenthal, Elizabeth Gore, Mitchell Machtay, William Sause, James D. Cox

Manuscript received June 14, 2010; revised July 22, 2011; accepted July 26, 2011.

Correspondence to: Walter J. Curran Jr, MD, Department of Radiation Oncology and Winship Cancer Institute, Emory University, 1365C Clifton Rd, NE, Ste C4104, Atlanta, GA 30322 (e-mail: wcurran@emory.edu).

J Natl Cancer Inst 2011; 103: 1452-1460

Concurrent vs Sequential Chemo/RT: RTOG 9410



RTOG 9410: Outcomes

	Sequential CRT	Concurrent CRT QD	Concurrent CRT BID
Median Survival Times (mo)	**14.6**	**17.0**	**15.6**
Overall Survival (5yr)	**10%**	**16%* (p=0.046)**	**13%**
Response Rate	61%	70%*	65%
Complete Response Rate	30%	42%	33%

* = statistically different compared to Arm 1

RTOG 9410: Toxicity

	Sequential CRT	Concurrent CRT QD	Concurrent CRT BID
Acute esophagitis (grade 3+)	**4%**	**22%* (p < 0.001)**	**45%*^ (p < 0.001)**
Late Esophageal toxicity (grade 3+)	**1%**	**3%**	**4%**
Acute Pulmonary (grade 3+)	**9%**	**4%**	**2%**
Late Pulmonary (grade 3+)	**15%**	**13%**	**17%**

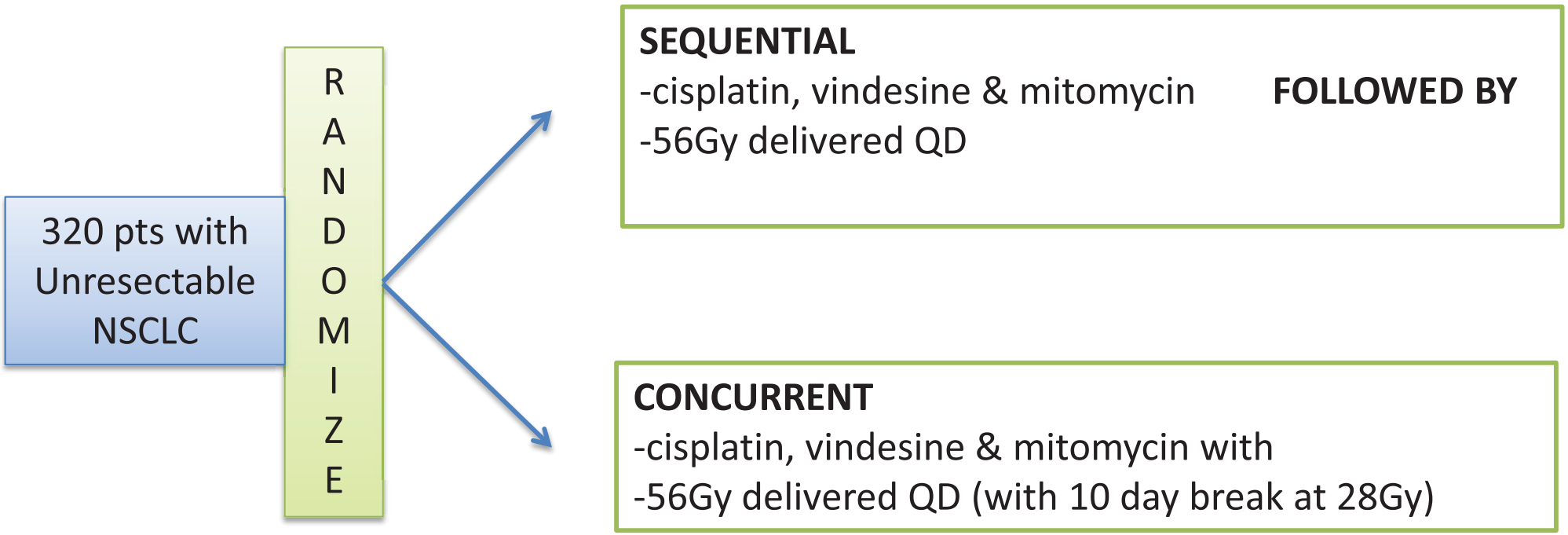
* = statistically different compared to Arm 1
^ = statistically different compared to arm 2

RTOG 9410: Conclusions

- Concurrent chemo/RT with cisplatin-based chemo improves survival over sequential treatment
  - Worse acute toxicities but equivalent late toxicity
  - Benefit likely from radiosensitization of chemo

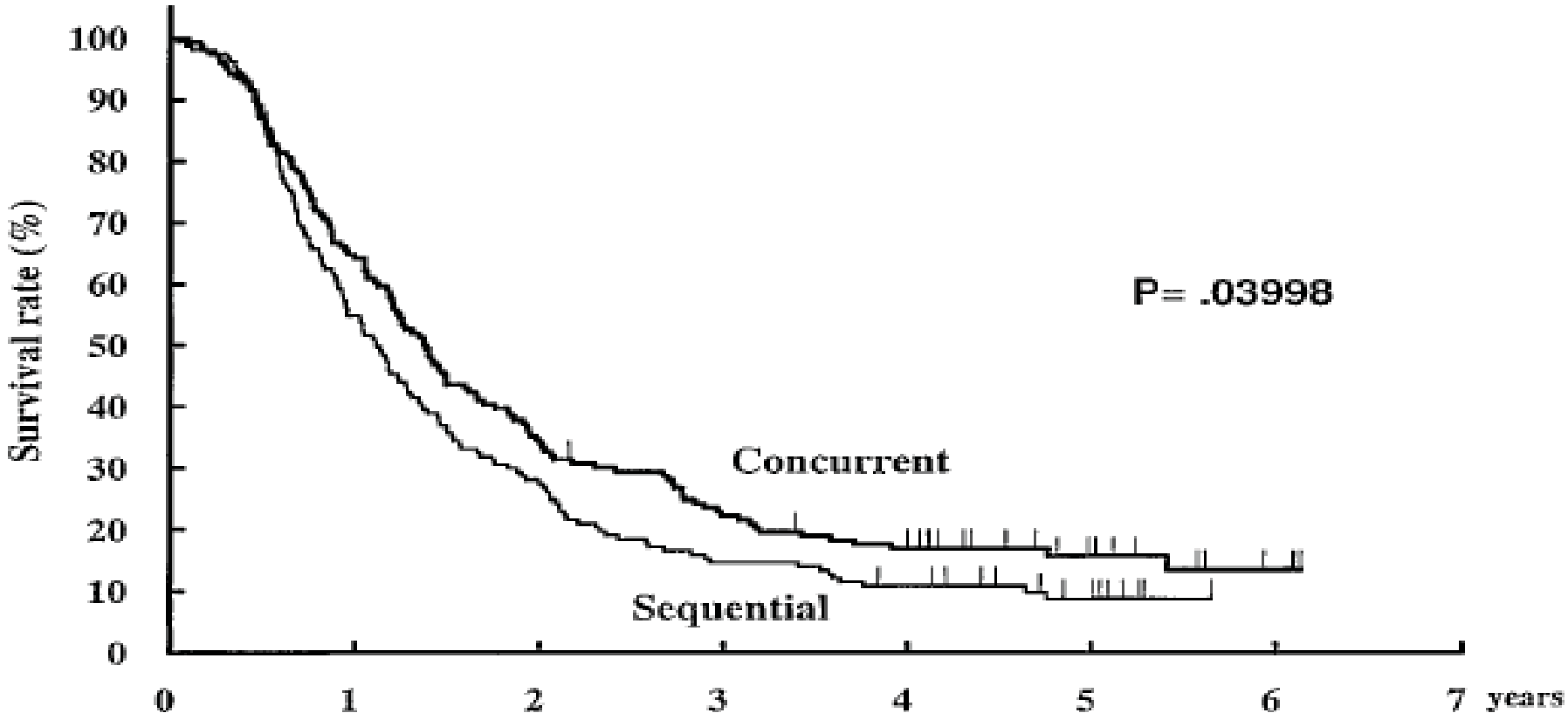
- QD radiation as good or better than BID
  - Radiosensitization benefit diminished by higher toxicity

Support for RTOG 9410: Furuse, JCO, 1999



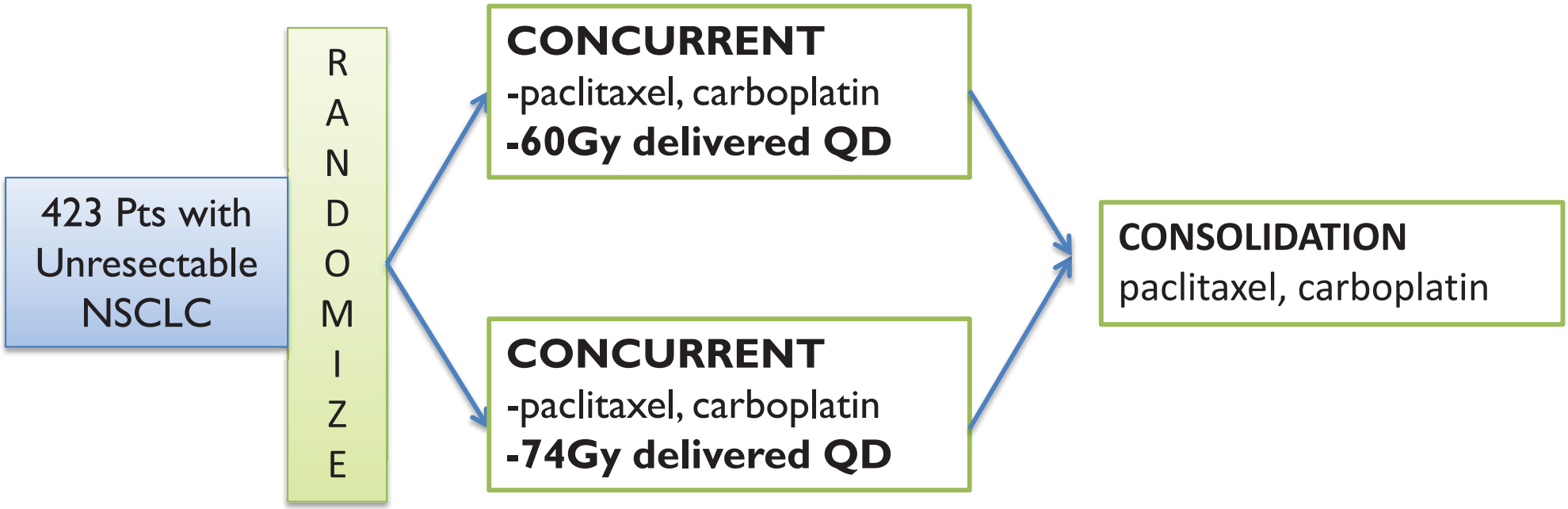
Furuse: Results

- Median OS 16.5 vs 13.3 months in concurrent and sequential arm
- No difference in Esophagitis



Radiation Delivery

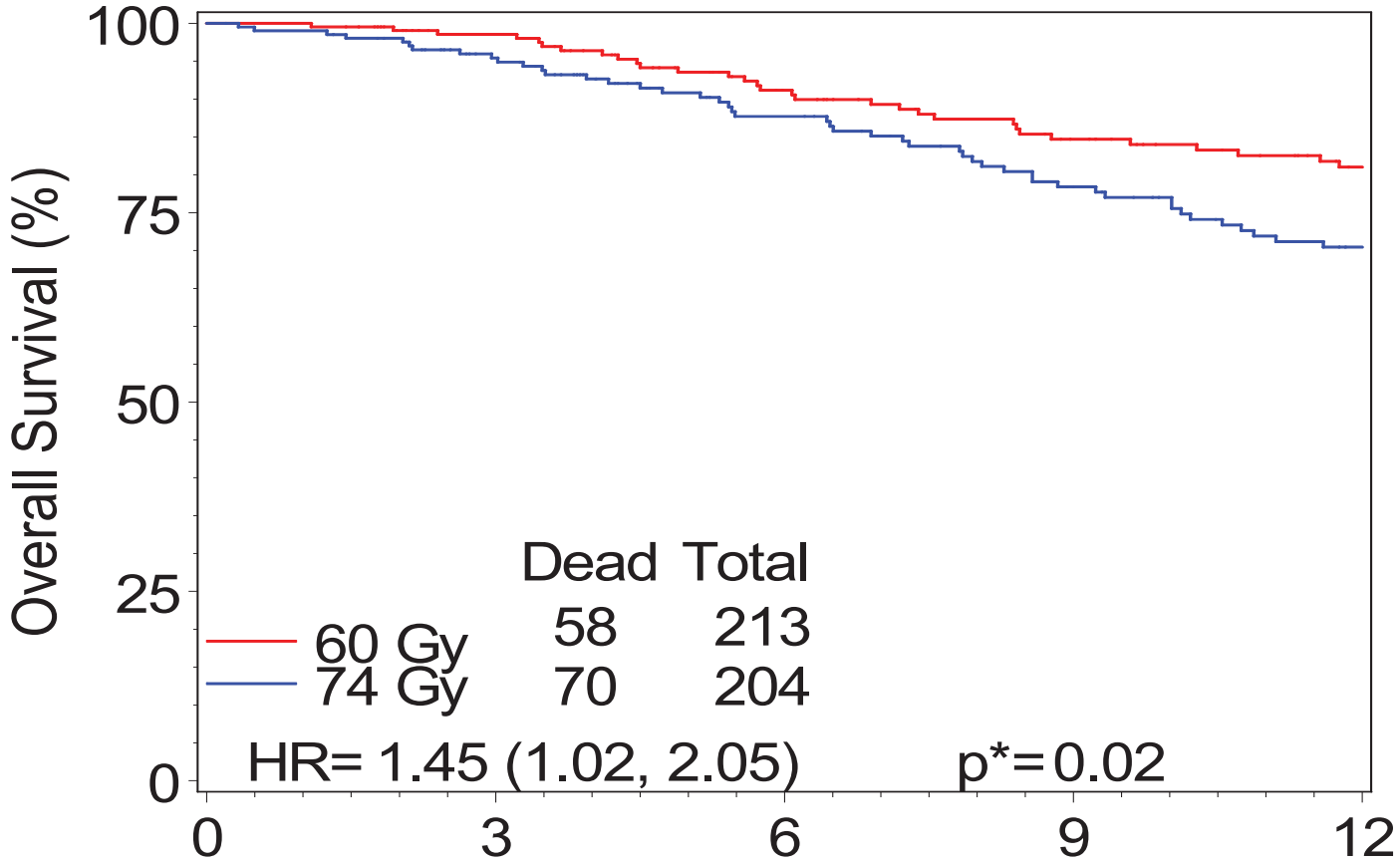
Dose Escalation: RTOG 06-17



Eligibility:

- Surgically unresectable stage III NSCLC
- Histologically confirmed
- PS 0-1, <10% weight loss
- FEV1 >= 1.2 L/sec
- No N3/SCV disease, prior therapy

RTOG 06-17: Prelim Results



Patients at Risk					
60 Gy	213	190	149	124	104
74 Gy	204	175	137	116	93

*One-sided p-value, left tail

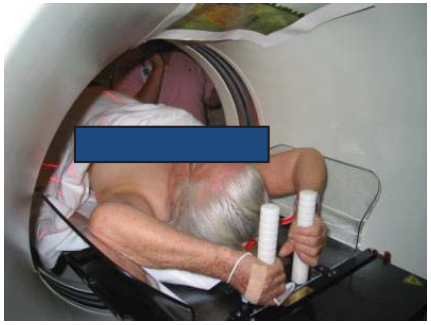
*8 Grade 5 events in 74 Gy Arm vs. 4 events in 60 Gy arm

RTOG 06-17: Other findings

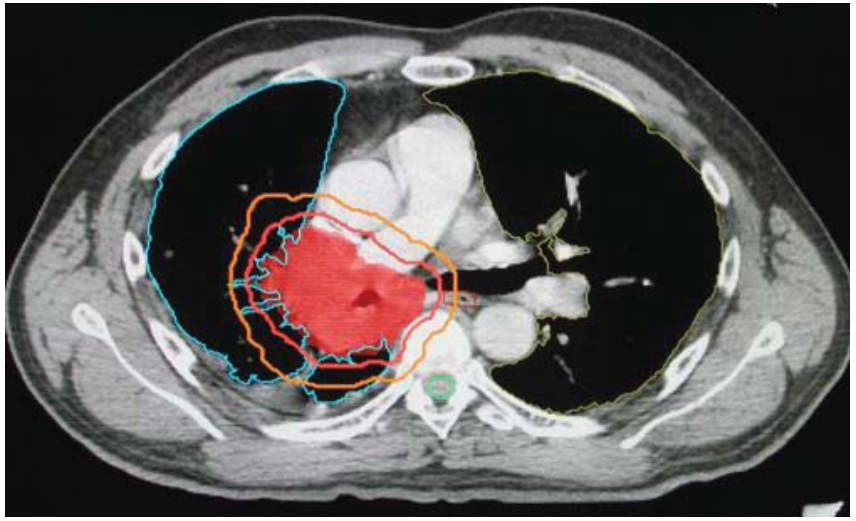
- On MVA: decreased RT dose, increasing GTV size, and non-squamous histology associated with improved survival
- GTV sizes smaller in 74 Gy arm
  - Potentially missing target in high-dose arm?
- More non-squamous in 60 Gy arm:

3D Simulation & Planning

- CT scan in Radiation Oncology Department
- Patient set-up in treatment position = simulation: supine/flat, arms up, free-breathing, iv contrast



- Tumor and normal tissues are outlined on CT scan



Potential designs:

- ~40 Gy AP/PA ➔ 20 Gy off-cord obliques
- 4-fields throughout AP/PA/opposed obliques off cord to 39.6-45 Gy, then cone down

Organs	**"Reasonable" dose constraints**
Lungs	**V20 = 35**-40% for both lungs* V5 = 45-65% **MLD <= 20 Gy**
Esophagus	minimize V60 (10-30%) max 70 Gy
Heart	**V40 ~ 40%** left ventricle V40=10%, max 50 Gy
Spinal cord	**max 45-50 Gy** (consider margin)
Brachial plexus	**max 60 Gy** (66 Gy ok)

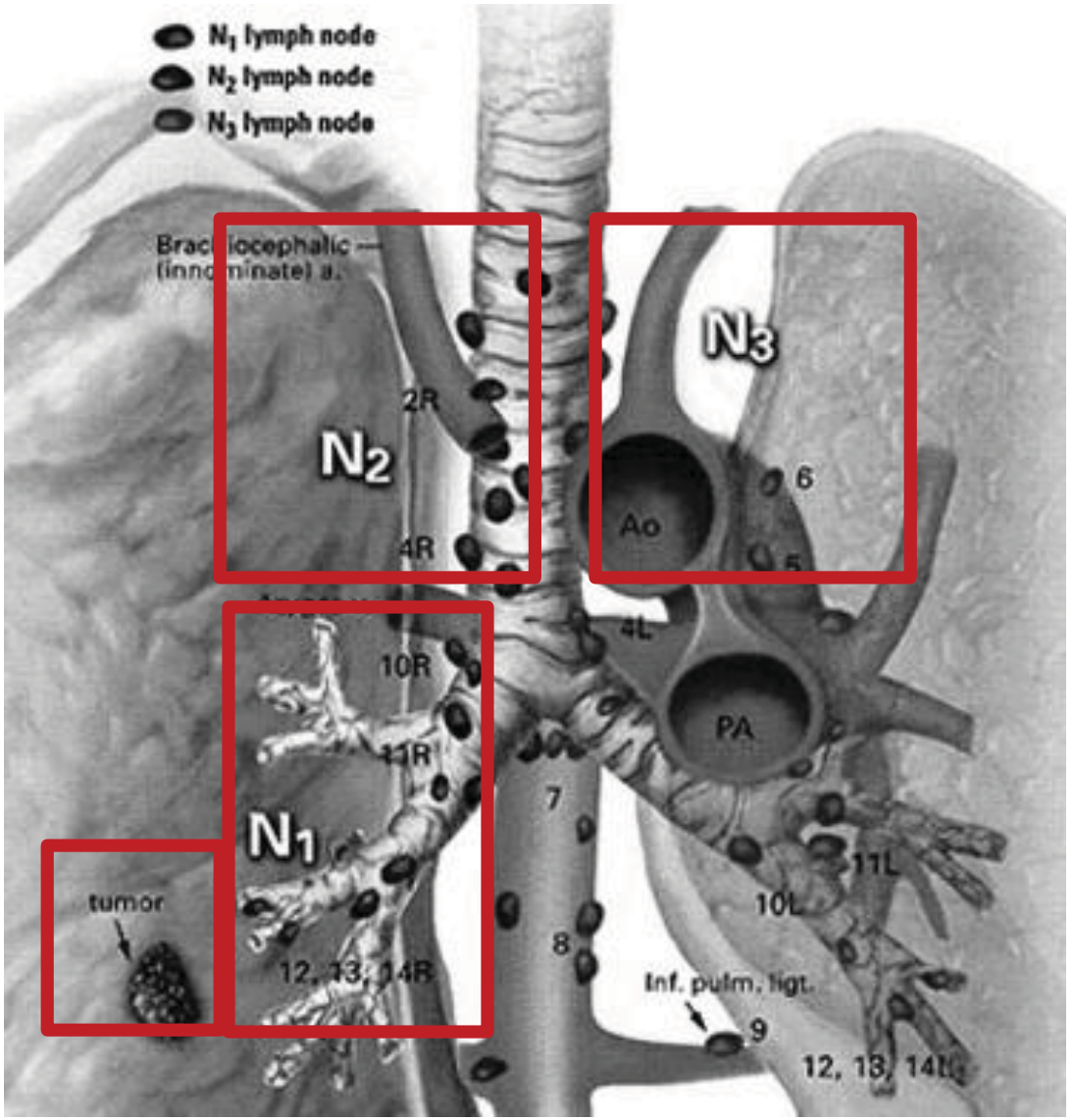
*lungs minus ITV, CTV, or PTV

Non-Small Cell Lung Cancer Staging

- History and physical examination
- Laboratory testing - Complete blood count, Electrolytes, Calcium, ALP, Albumin, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Total bilirubin, and Cr.
- Computed tomography (CT) of the chest with intravenous contrast
- CT plus PET
- Brain MRI

Silvestri, Chest 2007: 132:178S

Lymph Nodes (LN)



- N0: Zero LN Involved — 42%
- N1: Ipsilateral Hilar Lymph Nodes — 29%
- N2 Nodes: Ipsilateral mediastinal and/or subcarinal lymph nodes — 16%
- N3 Nodes: Contralateral mediastinal, contralateral hilar, supraclavicular, or scalene lymph nodes — 7%

Chest 2007: 132:178S

PET/CT Study

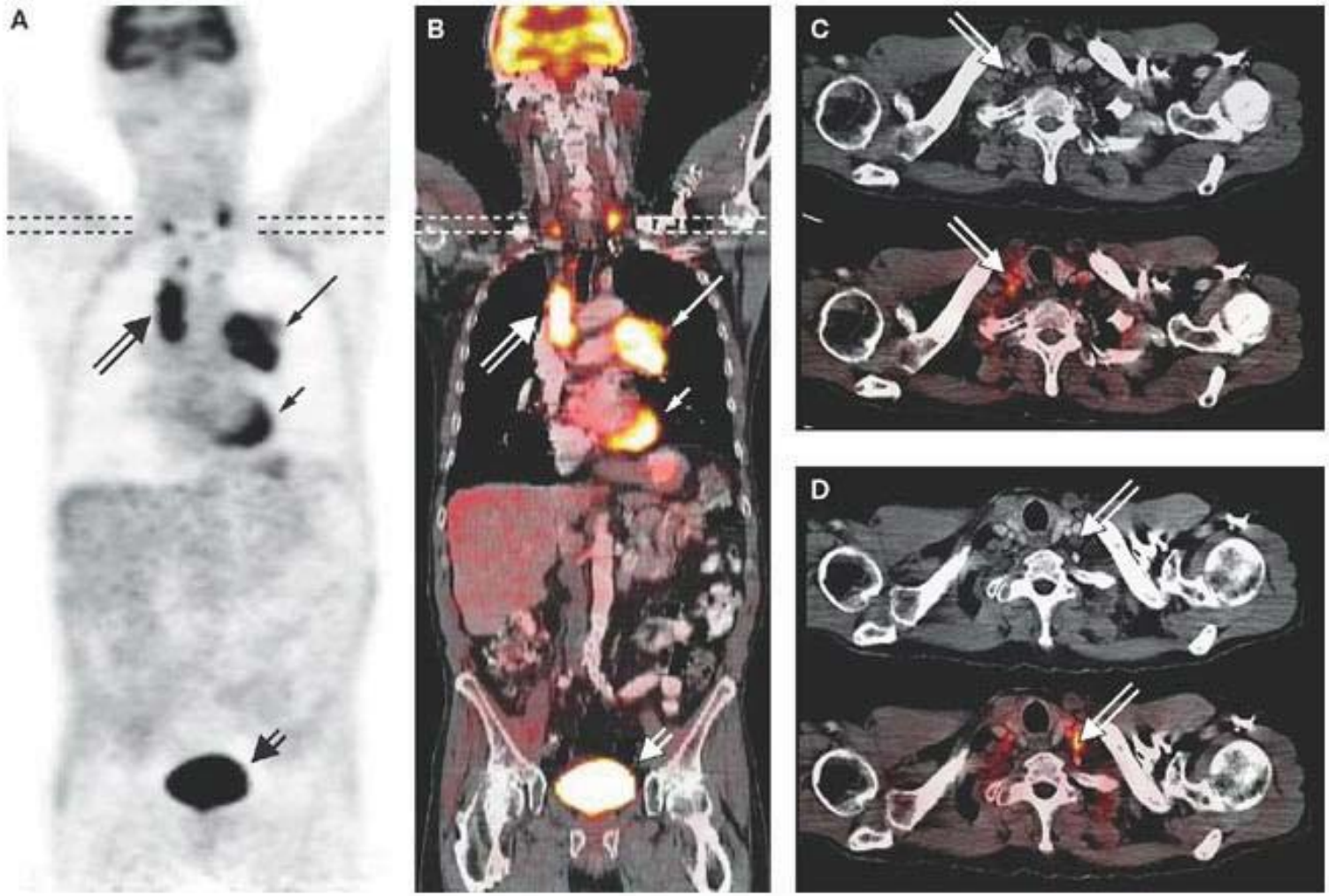
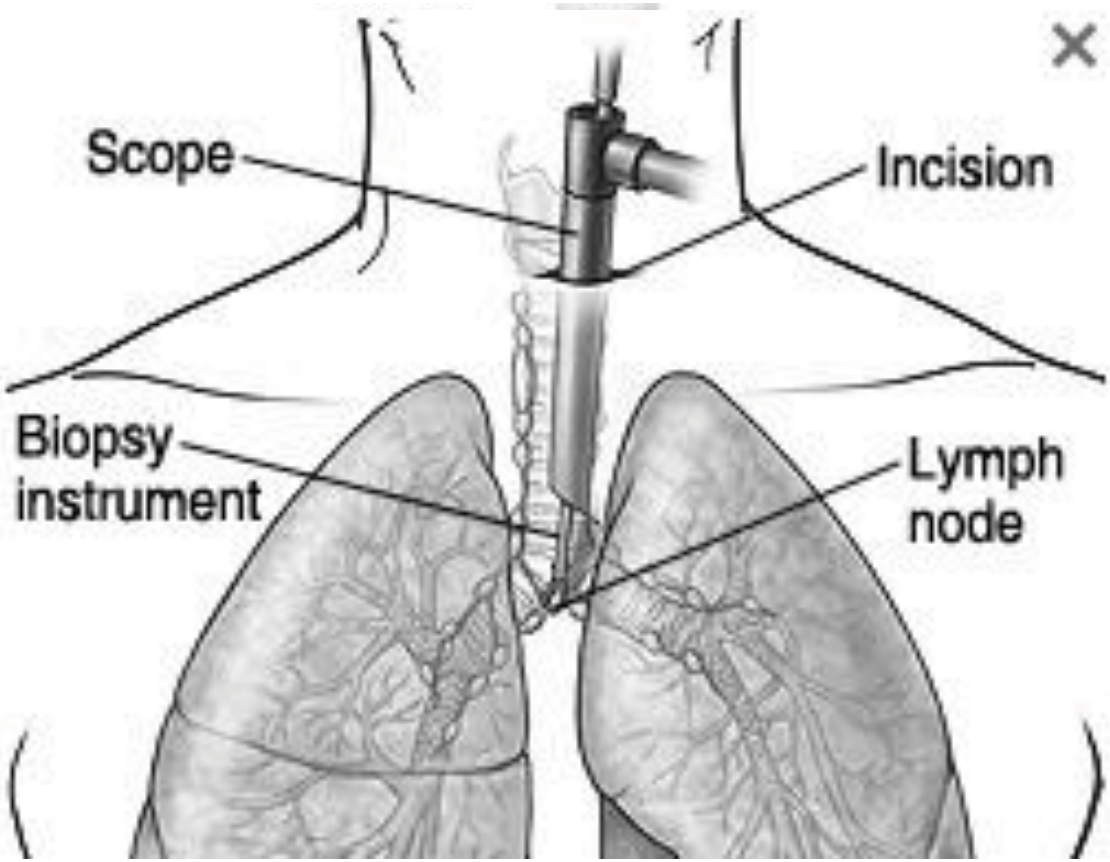


Figure 2. PET/CT study in a patient with non-small-cell lung cancer.

Nature Clinical Practice Oncology (2008) 5, 160-170

Lymph Node Sampling



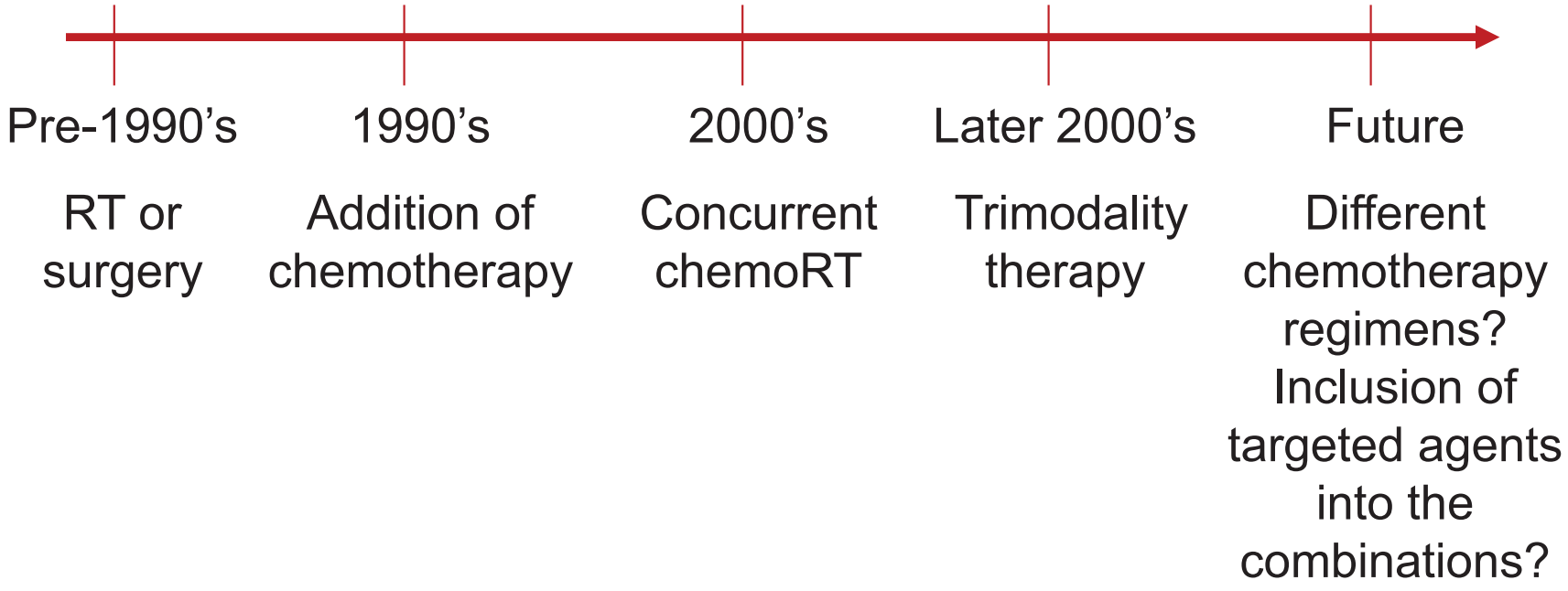
- Mediastinoscopy is a surgical procedure. Able to sample paratracheal, anterior subcarinal and bilateral hilar nodes
- Endobronchial ultrasound is less invasive. Able to sample paratracheal, subcarinal, and hilar lymph node stations

Chest 2007: 132:178S

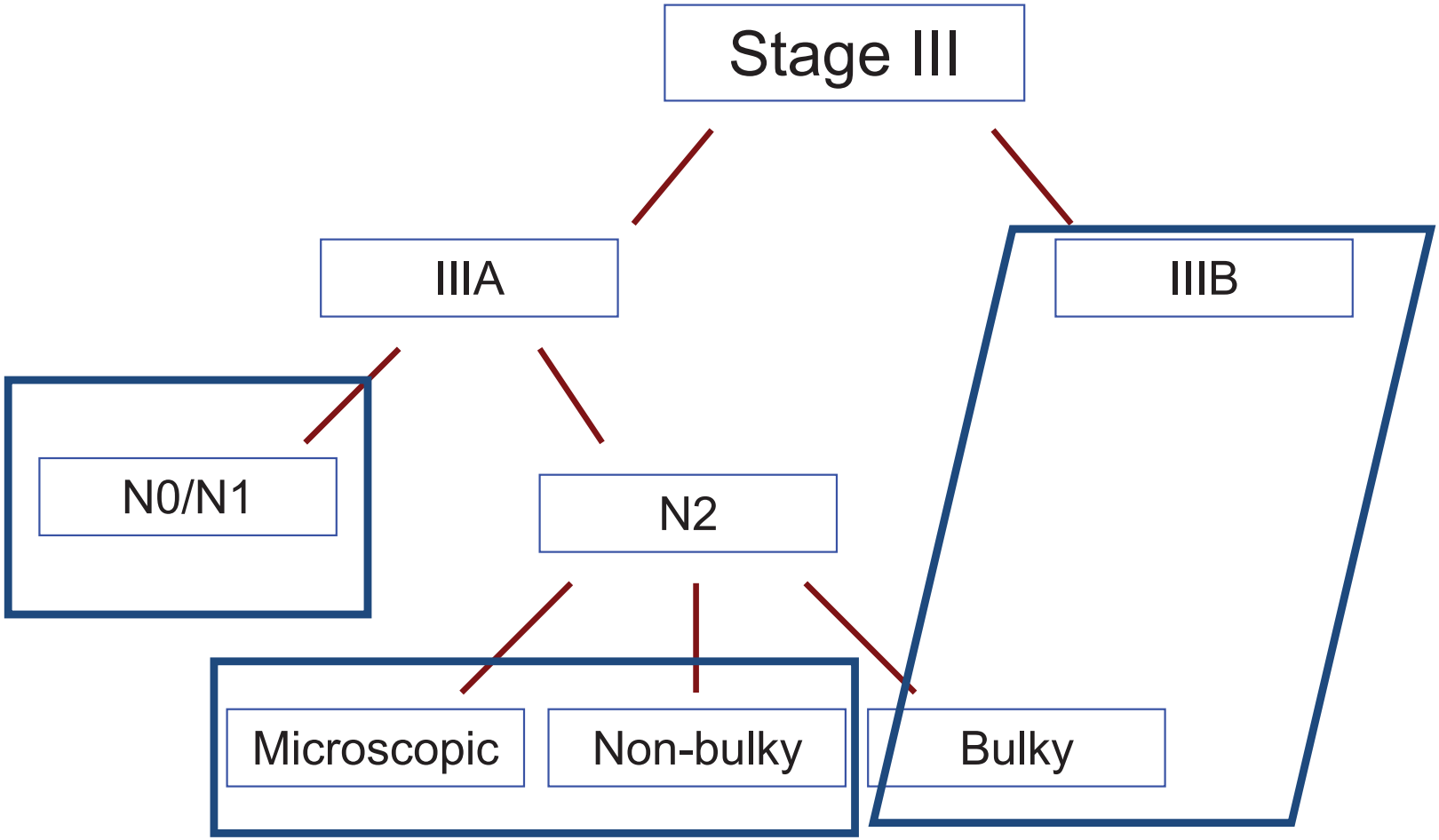
Summary Regarding Staging

- History and Physical
- Labs
- CT with Contrast
- PET accuracy is 78% for initial staging. Has a negative predictive value of 90%. However, mediastinoscopy is gold standard.
- Mediastinoscopy upstages the patient 15% of time and downstages 5% of time. We generally offer a mediastinoscopy unless there is a small (< 2 cm) peripheral tumor.
- Staging is necessary to correctly identify the patient's clinical-diagnostic stage and potentially spare the patient from unnecessary treatments (radiation, surgery)

Management of Stage III NSCLC



What is Stage III?



Also to consider:

- Overall health of patient
- Operable vs inoperable

Chemotherapy for Stage III Disease

- Concurrent chest irradiation and cisplatin-based chemo
- EP50/50 Regimen is Etoposide and Cisplatin (Based on SWOG 8805 and 9019 studies)
- Etoposide 50 mg/m2 IV bolus days 1,2,3,4,5
- Cisplatin 50 mg/m2 days 1,8
- Premedication: Mannitol 25% 12.5 gm IV qD on d1,8 + Furosemide 20 mg IV on d1,8
- IV Hydration

Albain KS, SWOG 8805. *J Clin Oncol* 1995; 13: 1880–92.
Albain KS, SWOG-9019. *J Clin Oncol* 2002; 20: 3454–60.
Albain KS. *Lancet* 2009; 374: 379–86

Side Effects

- Cisplatin (cross-links and interferes with the function of DNA) – Allergic reaction, Bone marrow suppression, GI toxicity, Ototoxicity, Nephrotoxicity

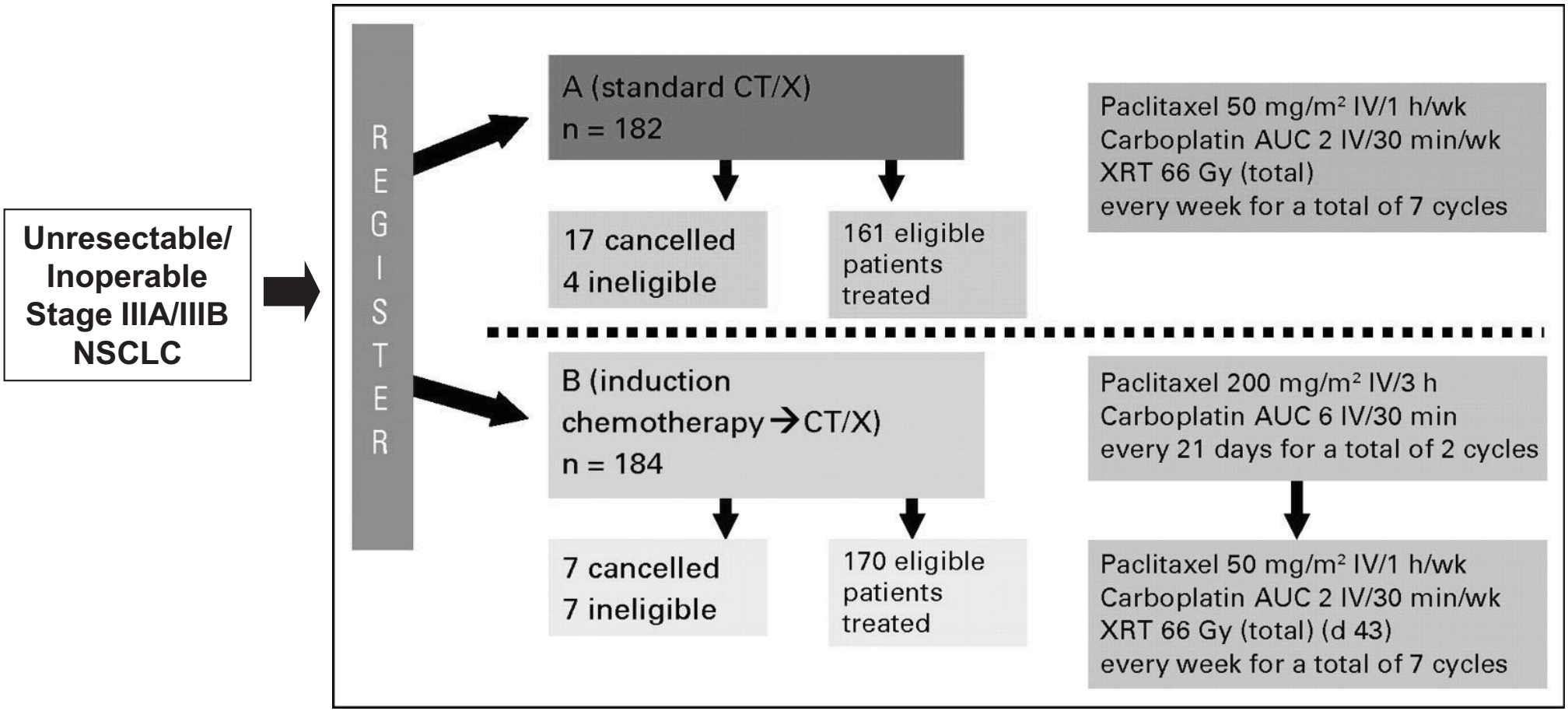
- Etoposide (topoisomerase II inhibitor which acts at the premitotic stage of cell division to inhibit DNA synthesis) – Allergic reaction, Bone marrow suppresion, Hepatoxcity, Acute leukemia (rare)

Anti-emetic Regimen

- Anti-emetic Therapy Ondansetron 16 mg PO or IV Day 1,8 of each cycle
- Dexamethasone 12 mg PO or IV Day 1,8
- Aprepitant 125 mg PO qD followed by 80 mg on Day 2,3 each week
- Lorazepam .5-1 mg Q3 H PO or IV for nausea
- Home medications – Ondansetron, Compazine, Decadron, and Ativan

Induction with Weekly Carbo/Taxol

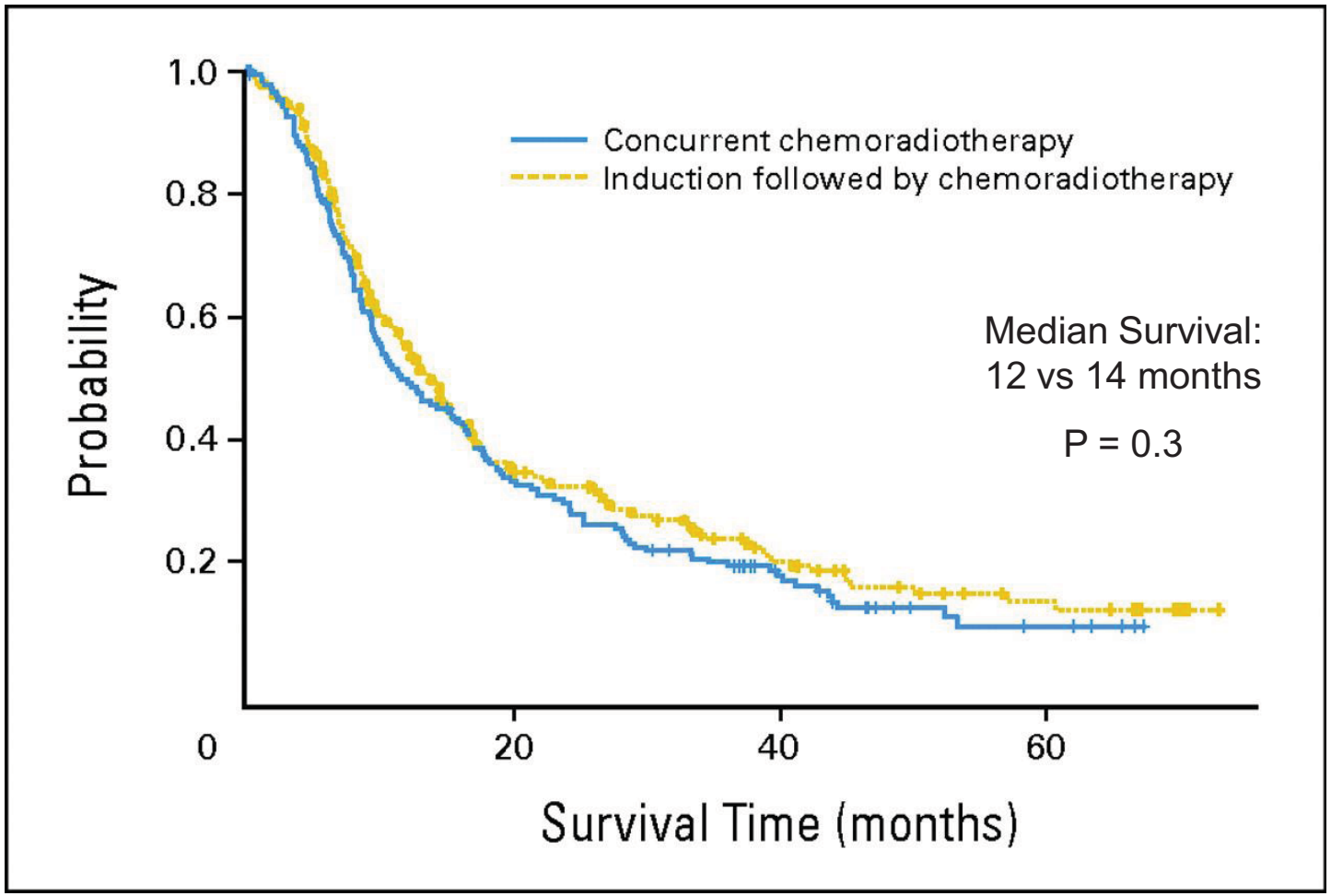
CALGB 39801



Vokes EE, et al, JCO 2007

Induction with Weekly Carbo/Taxol

CALGB 39801

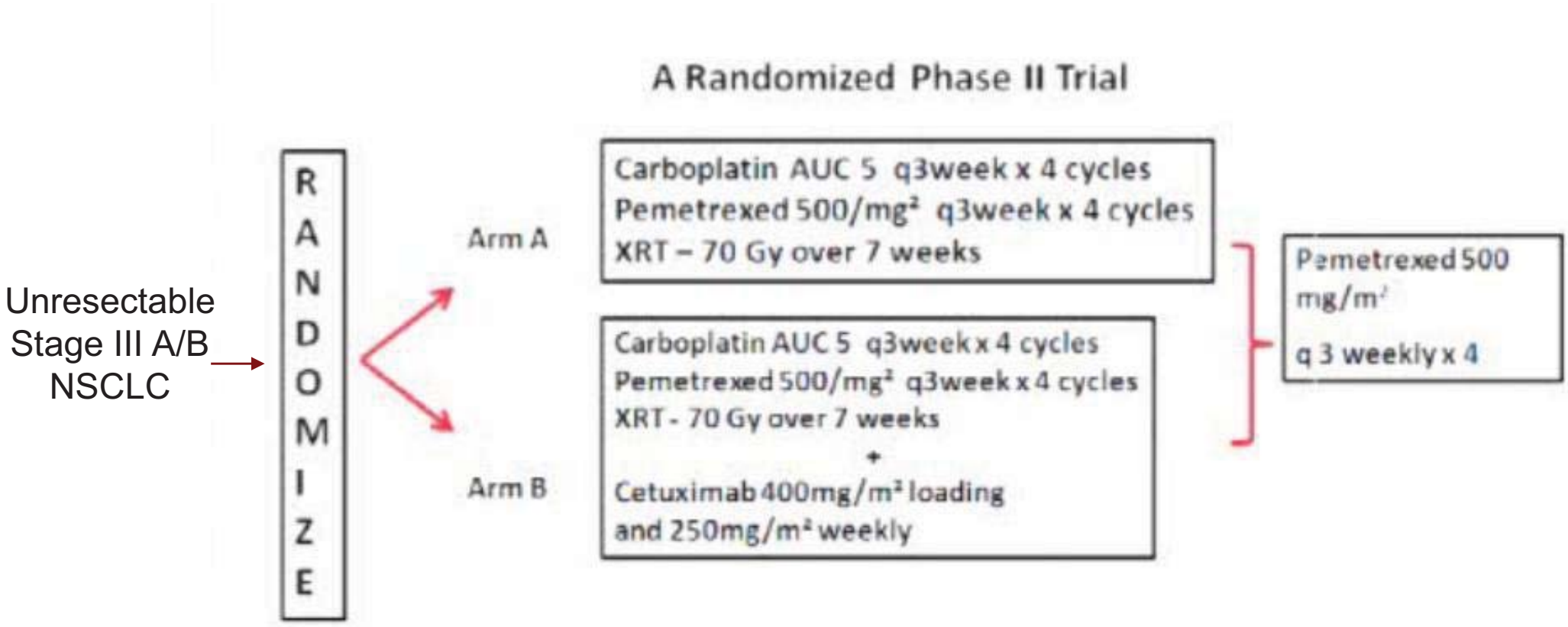


Vokes EE, et al, JCO 2007

Pemetrexed

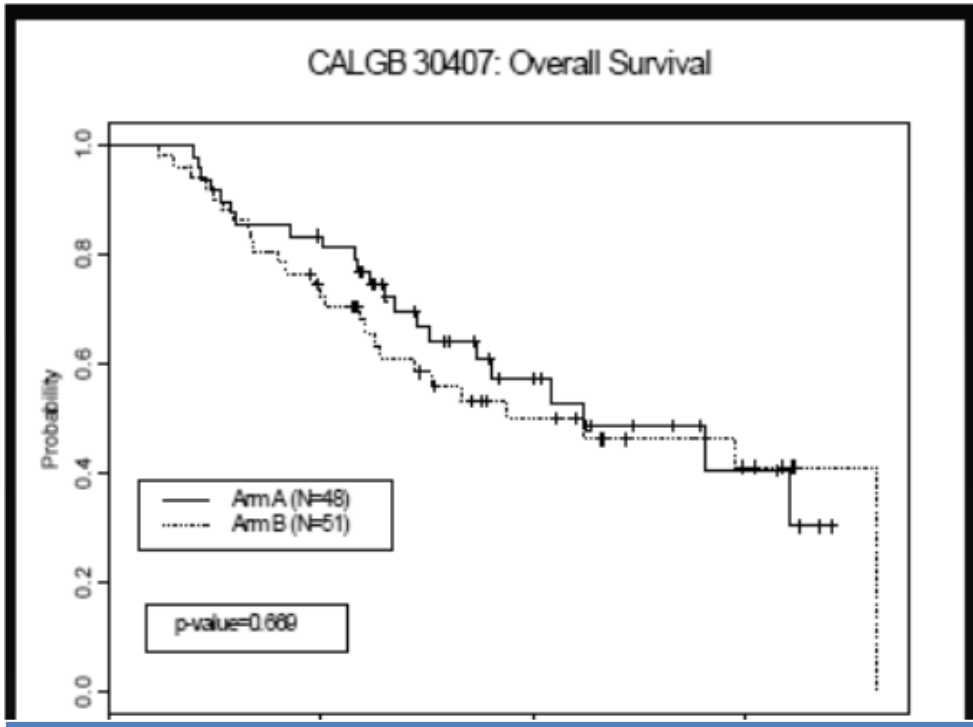
- Pemetrexed (antifolate that disrupts folate-dependent metabolic processes essential for cell replication) – skin reaction, GI distress, bone marrow suppression, fatigue, sensory neuropathy, renal failure, Acute Lung Injury
- Phase I data shows that pemetrexed is the 1st 3rd generation chemotherapy possible to deliver at full dose with RT
- CALGB 30407 (Phase II study) evaluated combination of Carboplatin-Pemetrexed with 70 Gy (OS 22 mon)
- PROCLAIM (Phase III study) will shed light on the effectiveness of Cisplatin-Pemetrexed with 66 Gy

CALGB 30407



Govindan R, et al, Abstr 7505, ASCO 2009

Carboplatin-Pemetrexed-70Gy



Median Overall Survival

Arm A 22 months (95% CI: 17-NA)
Arm B 22 months (95% CI: 13-NA)

18 Month Overall Survival

Arm A 57% (95% CI 44-75)
Arm B 50% (95% CI 37-68)

Grade 3-5 toxicty:

Esophagitis 30%

Pneumonitis 10%

Mortality 4% (pulmonary)

Govindan R, et al, Abstr 7505, ASCO 2009

PROCLAIM Clinical Trial On-Going