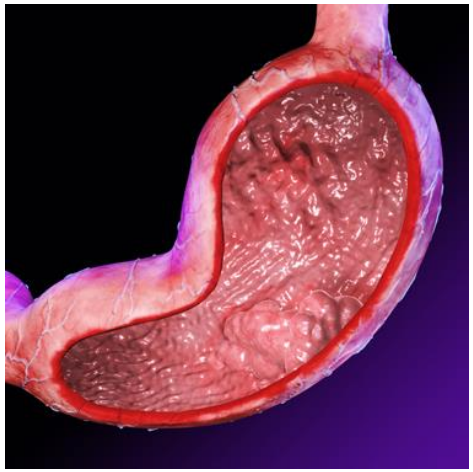
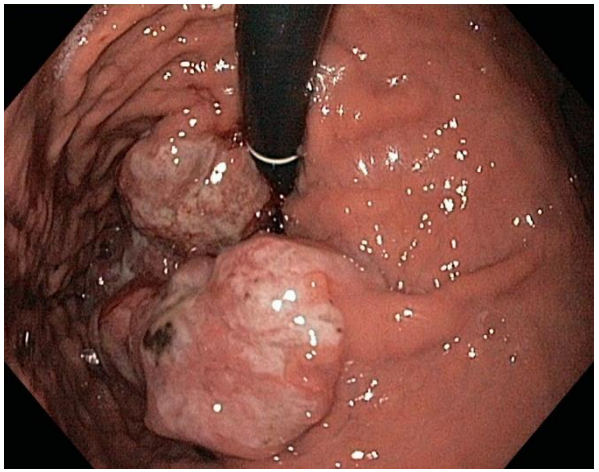
Gastric Adenocarcinoma

Bible Class Stefan Christen
31.07.2019 Bern



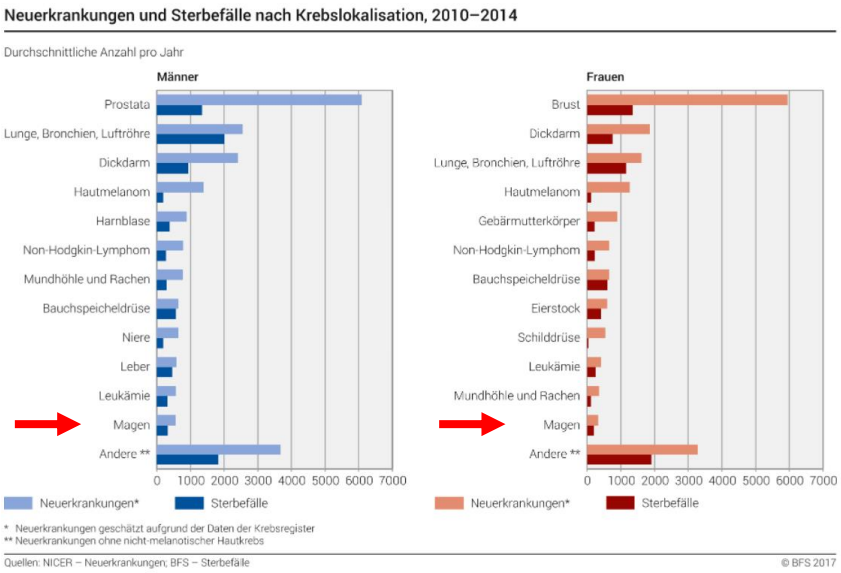


Epidemiology

Epidemiology

- 700 new cases per year
- Constantly falling since 1986 : in Switzerland -6% due to the HP eradication for the intestinal type, augmetation of diffuse type

- Until 1980 most common cause of death by cancer.
- 5th most common cancer worldwide
- 3 rd cause of mortality worldwide
- High incidence in Asia (China, Japan and Korea) eastern Europe, South America
- 5 year survival around 27%, 80% in early cancer



Bundesamt für Statistik 2017

Malvezzi M. Ann Oncol. 2016 Apr;27(4):725-31.

Köberle D. Schweiz Med Forum 2013;13(21):397–400.

Riscfactors

Riscfactors

- **Alimentary:** Alcohol, tabaco, high salt intake, nitrate
- **Infectious:** HP (Risk 2-3↑), EBV+ status
- **Ethnicity:** Asian>Black and Hispanic-Latino>White
- **Genetic:** Lynch syndrome, Peutz Jeghers, FAP, juvenile polyposis
- **Hereditary diffus castric carcinoma** (1%, germline mutation of CDH-1-Gen (E-Cadherin+) - life-time-risk 80%!)
- **Predisposing conditions:** partial gastrectomy >10 y, M. Ménétrier

Genetic testig in susceptible individuals

Box 1 Criteria for referring to genetic services

Suspected familial gastric cancer

- Gastric cancer in one family member before age 40.
- Or gastric cancer in two first-degree/second-degree relatives with one diagnosis before age 50*.
- Or gastric cancer in three first-degree/second-degree relatives independent of age*.

Suspected hereditary diffuse gastric cancer

- One case of diffuse gastric cancer before age 40.
- Or two cases of gastric cancer regardless of age in two first-degree/second-degree relatives, at least one confirmed diffuse gastric cancer*.
- Or personal and family history of diffuse gastric and lobular breast cancers, with one diagnosis before age 50.
- A personal or family history of cleft lip/palate in a patient with diffuse gastric cancer.
- In situ signet ring cells or pagetoid spread on gastric biopsies.

*In order to account for significant family history, the affected relatives need to be within the same side of the family (maternal or paternal).

- APC/MUTHY assoc. Polyposis
- juvenile polyposis -SMAD4 or BMPR1A mut
- Peutz-Jeghers - STK11/LKB1
- Cowden – PTEN
- Li-Fraumeni - TP53
- Gastric adennocarcinoma and Proximal polyposis of the stomach - exon 1B of APC gene

ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes
Syngal S et al. Am J Gastroenterol. 2015 Feb;110(2):223-62

Pathophysiology

Song H. BMJ. 2015 Jul 27;351:h3867.

Pathophysiology

Atrophic gastritis -> intestinal metaplasia ->epithelial dysplasia

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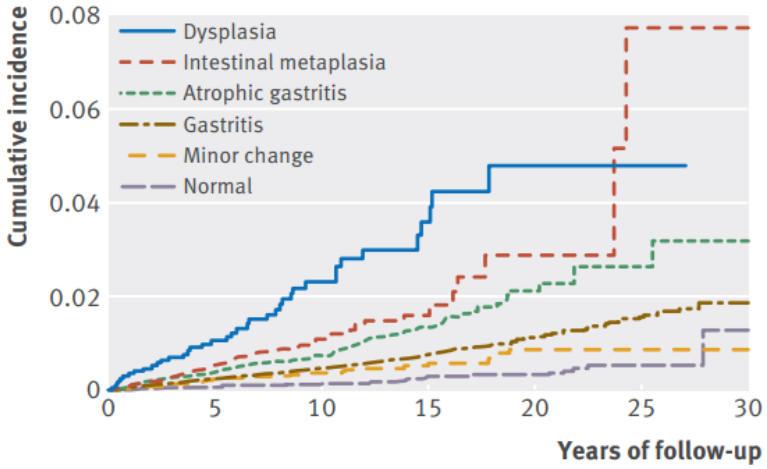
Song et al. 2015:
Gastroscopy biopsy in Sweden
405'172 Patients, 1979 to 2011

- 1'599 developed gastric cancer

Initial:

- 1/256 normal
- 1/85 gastritis
- 1/50 atrophic gastritis
- 1/39 intestinal metaplasia
- 1/19 dysplasia



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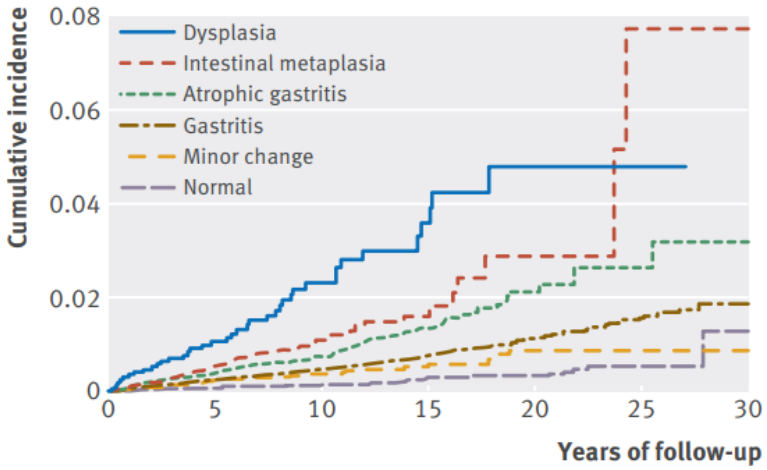

Table 3 The risk of cancer for patients with gastric atrophy and intestinal metaplasia

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All GA	1.9	0.1–0.5
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Intestinal metaplasia

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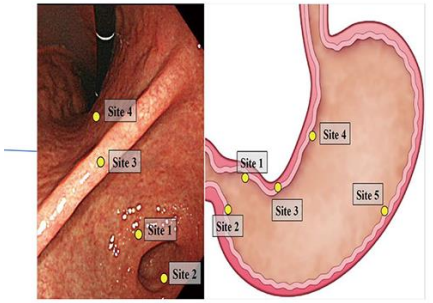
Sydney protocol biopsies



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- Complete vs Incomplete = colonic
  - Immunhistochemical
  - Risk for low grade dysplasia higher in incomplete metaplasia (complete 8% vs.31% incomlete metaplasia)

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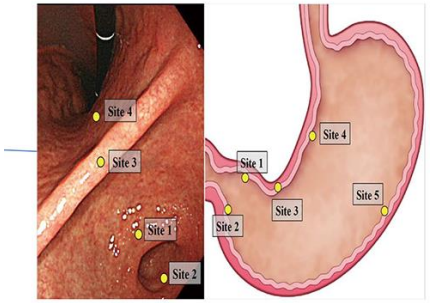

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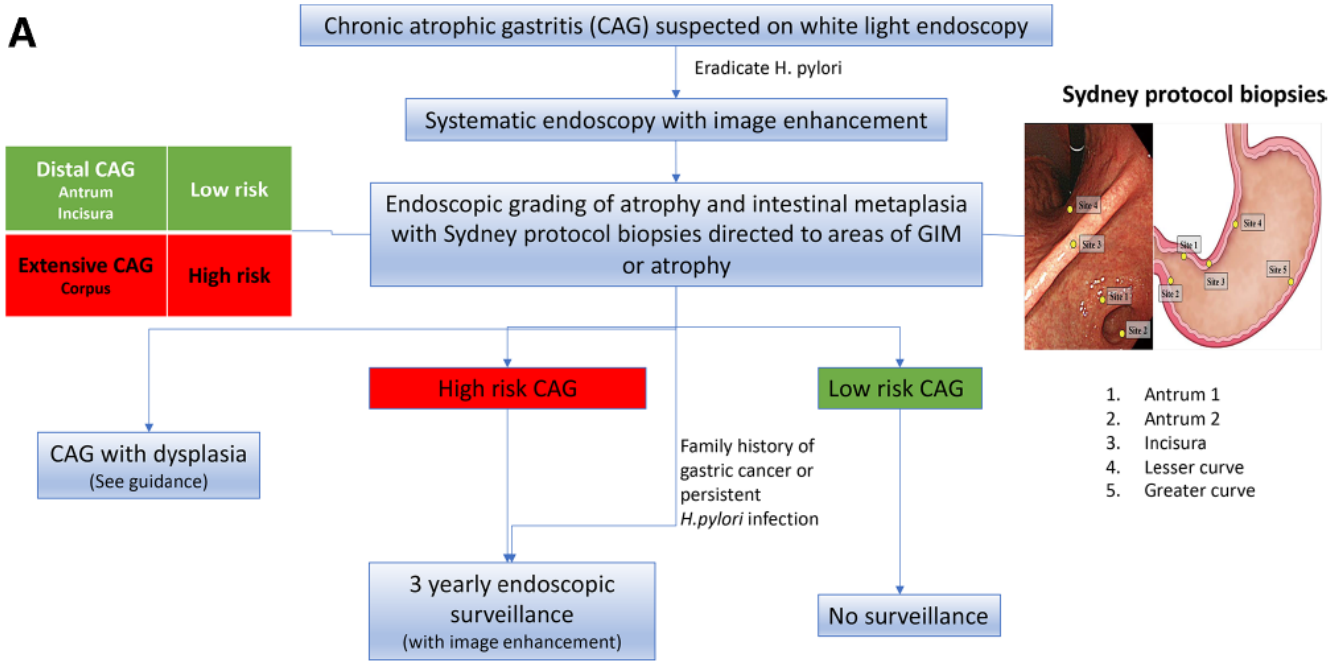
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Eradicate H. pylori
Systematic endoscopy with image enhancement
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Antrum
Incisura
Low risk
Extensive CAG
Corpus
High risk
CAG with dysplasia
(See guidance)
High risk CAG
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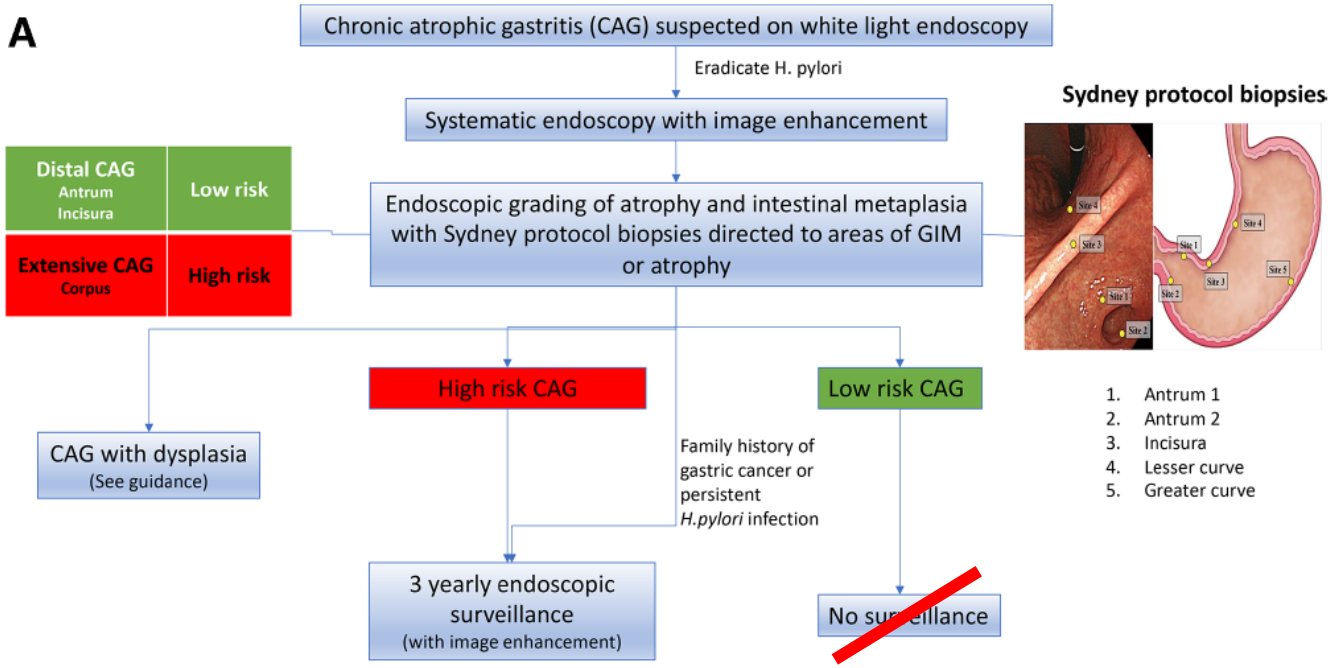
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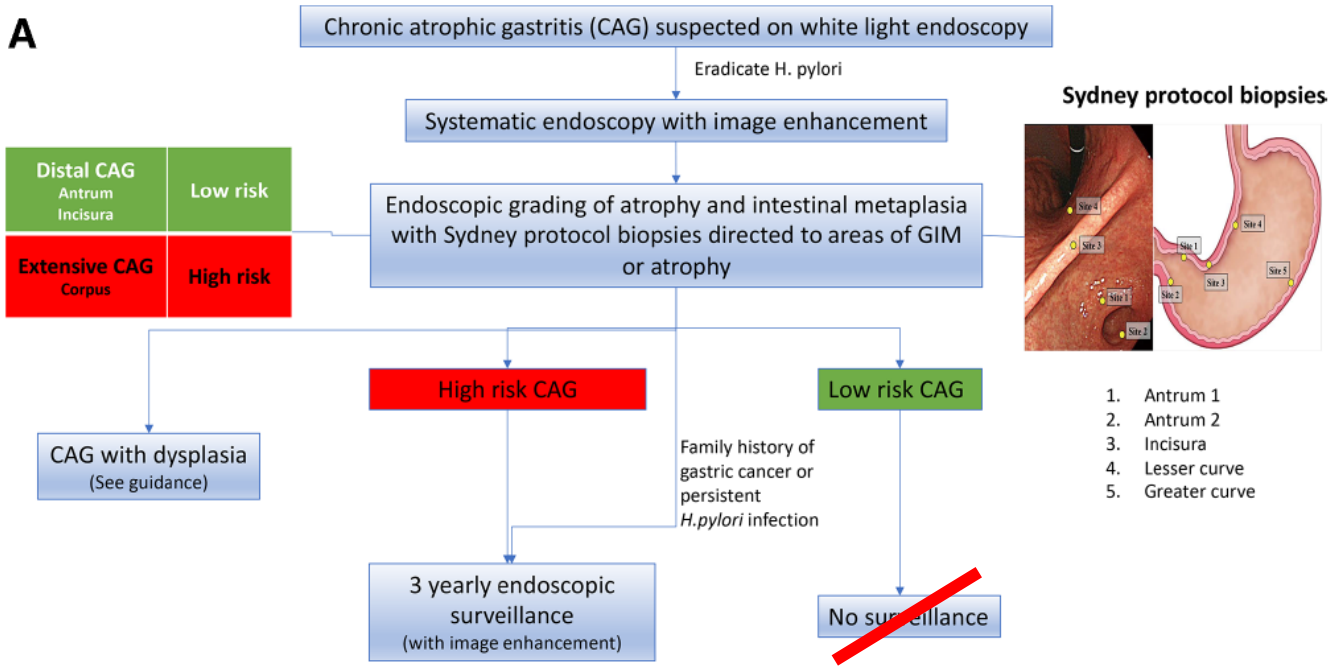
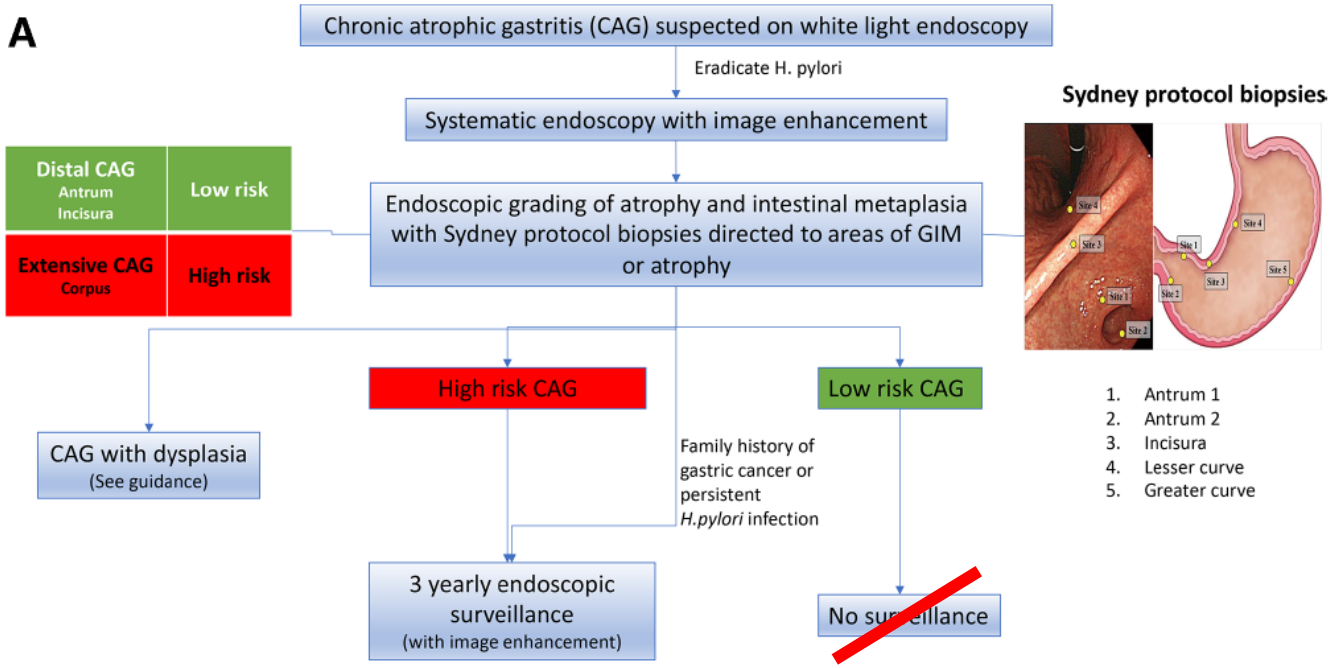


At Insel: 3 yearly endoscoic surveillance



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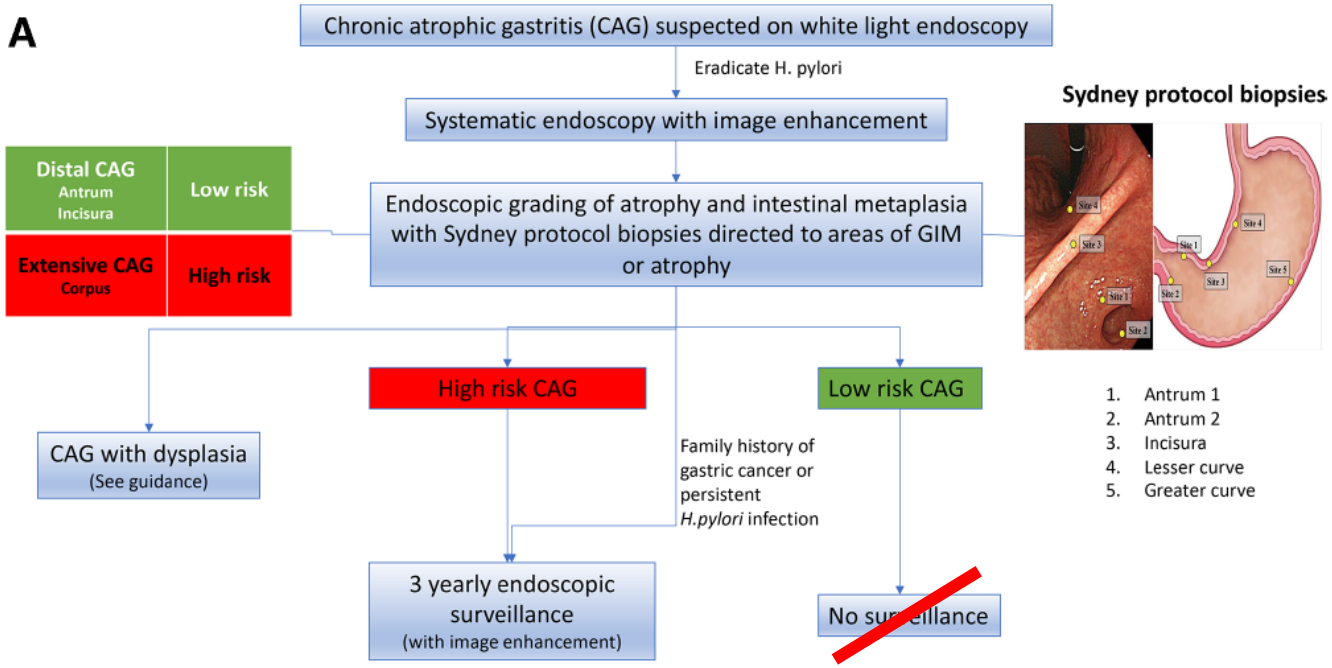

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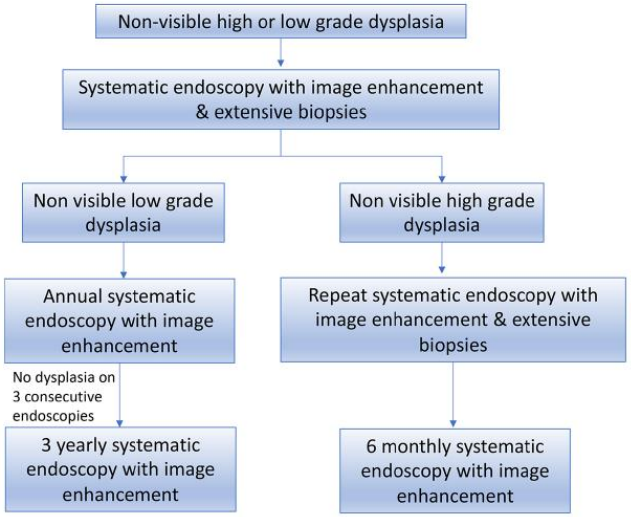

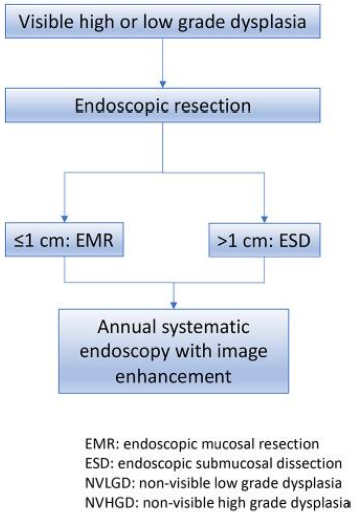

EMR: endoscopic mucosal resection
ESD: endoscopic submucosal dissection
NVLGD: non-visible low grade dysplasia
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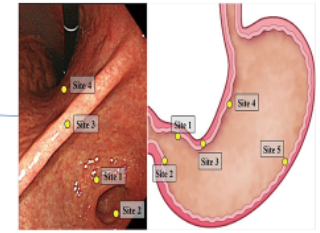

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CAG with dysplasia
(See guidance)

High risk CAG

Low risk CAG

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Non-visible high or low grade dysplasia

Systematic endoscopy with image enhancement & extensive biopsies

Non visible low grade dysplasia

Non visible high grade dysplasia

Annual systematic endoscopy with image enhancement

Repeat systematic endoscopy with image enhancement & extensive biopsies

No dysplasia on 3 consecutive endoscopies

3 yearly systematic endoscopy with image enhancement

6 monthly systematic endoscopy with image enhancement

Visible high or low grade dysplasia

Endoscopic resection

≤1 cm: EMR

>1 cm: ESD

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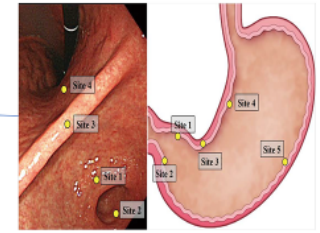

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What is the difference between HP pangastritis and predominant antral gastritis?

Which cell poduces acid in Stomach? Other important cells?

Cells of the stomach

Name	Region of stomach	Secretion	
Foveolar cells, Mucus neck cells	Fundus, Corpus, Antrum	Mucus gel layer	Protection uf mucosa
Parietal (oxyntic) cells	Fundus, Corpus	Gastric acid and intrinsic factor	
Chief (zymogenic) cells	Fundus, Corpus	Pepsinogen and gastric lipase	
D-Cells	Fundus, Antrum	Somatostatin	Inhibition of acid
G-Cells	Antrum	Gastrin	Stimulation of acid, peristaltic and grow of mucosa
ECL-Cells	Corpus	Histamain	Stimulation of acid

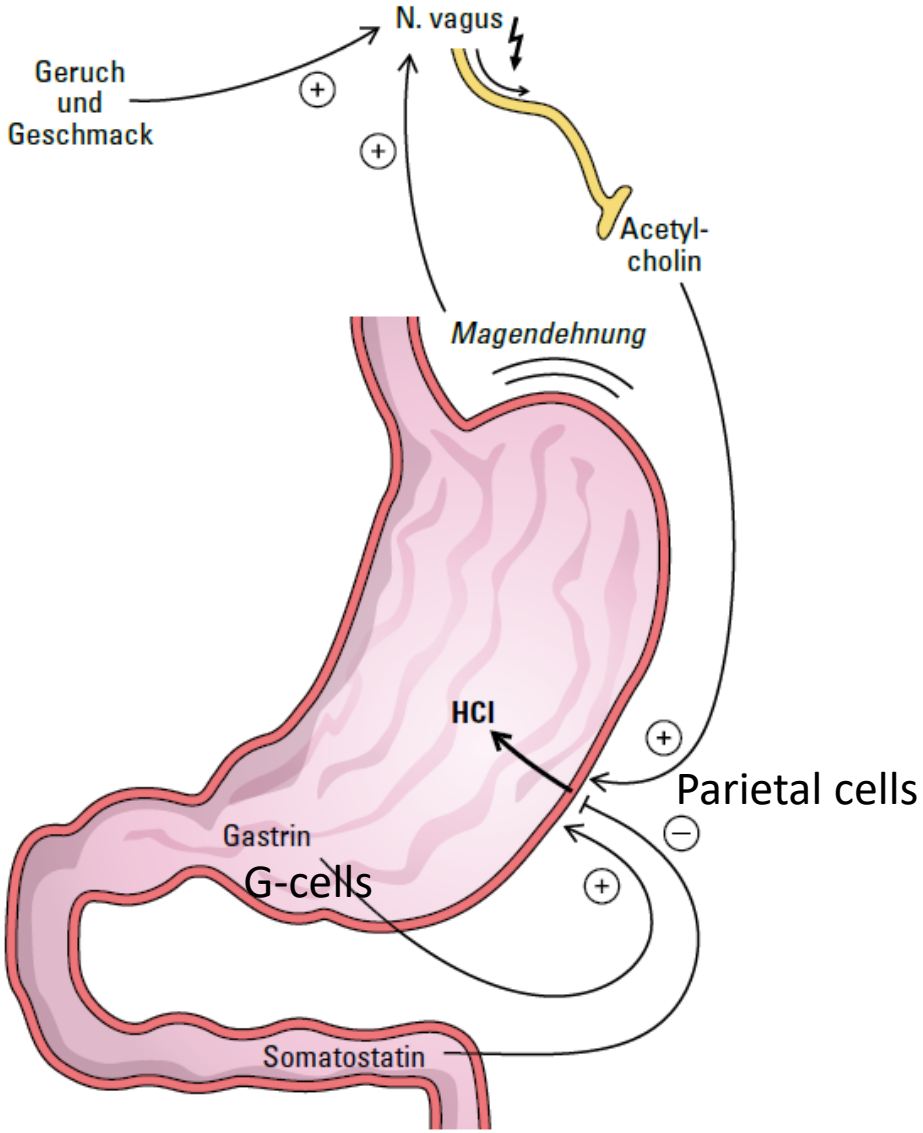
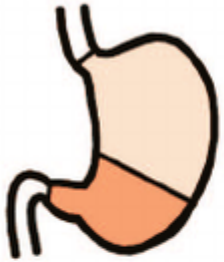
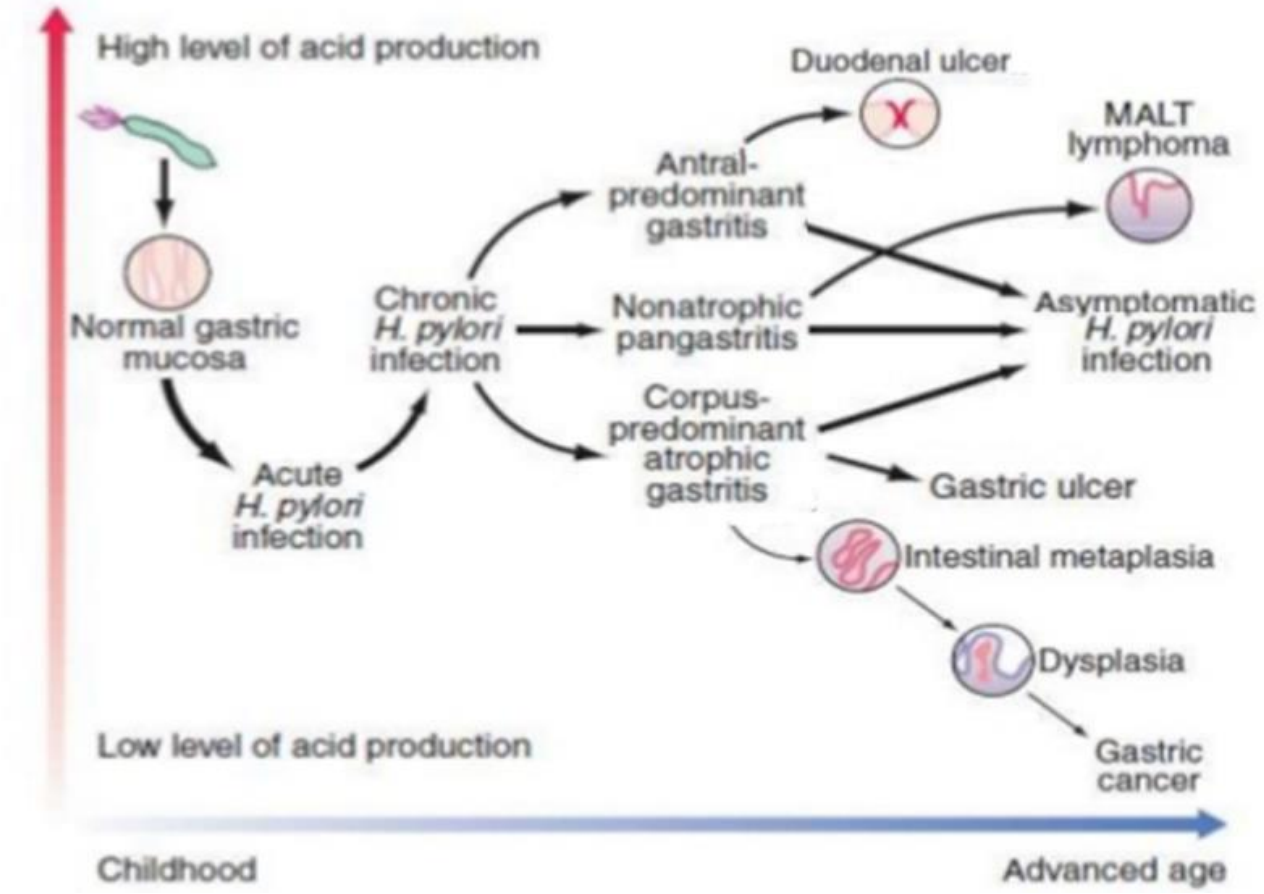


Abb. 20: Phasen der Magensäuresekretion

Helicobacter

Pattern of gastritis	*Gastric histology*	*Duodenal histology*	*Acid secretion*	*Clinical condition*
 Pan-gastritis	• Chronic inflammation • Atrophy • Intestinal metaplasia	• Normal	• Reduced	• Gastric ulcer • Gastric cancer
 Antral-predominant	• Chronic inflammation • Polymorph activity	• Gastric metaplasia • Active chronic inflammation	• Increased	• Duodenal ulcer

Natural history of H. pylori infection

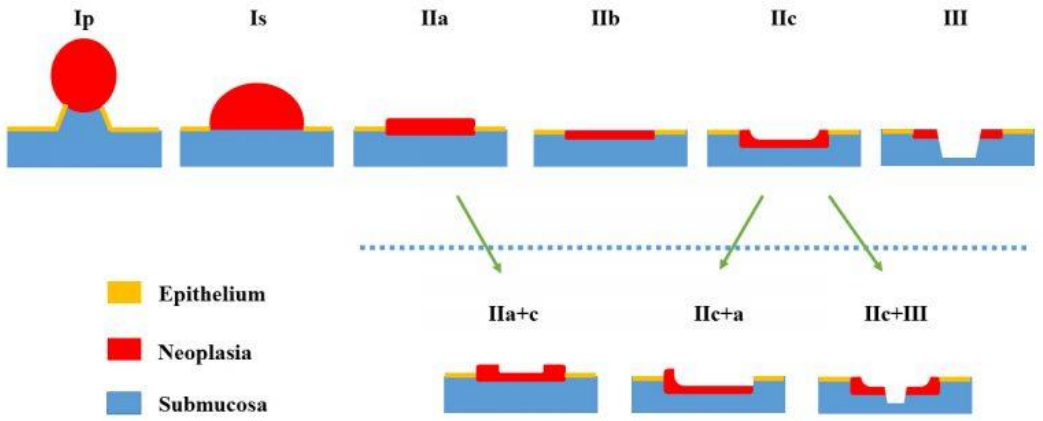


Diagnostic gastroscopy

Good Quality! Post endosopy cancer 11.3%!, at least 7min!

White light
Chromoendoscopy or virtual (NBI, FICE, i-scan)
Take 8-10 Biopsies

Paris Classification



The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon Gastrointest Endosc. 2003 Dec;58(6 Suppl):S3-43. Review

Classification by location

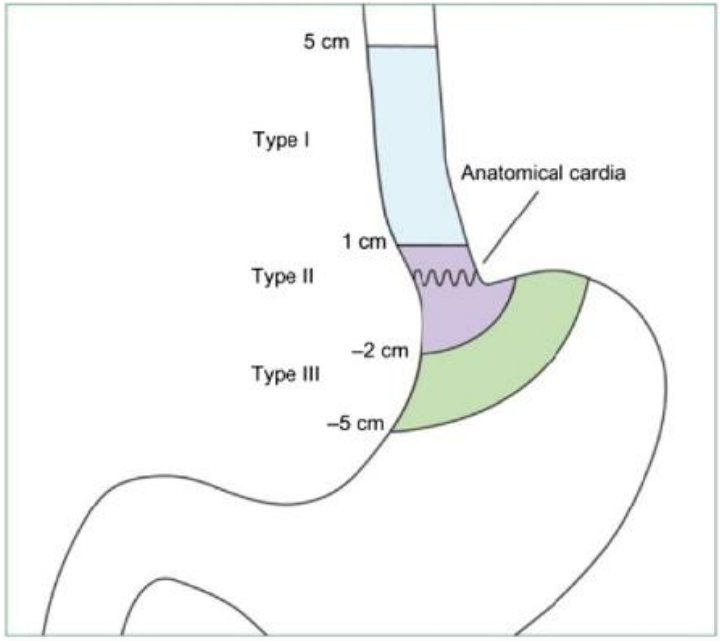


Fig. 1 The Siewert classification of GE junction adenocarcinomas.

Adenocarcinoma of esophagogastric junction = AEG

Typ I: Distal oesophagus out of intestinal metaplasia of the oesophagus

Typ II: Cardia, out of cardia epithel or intestinal metaplasia of the esophagogastric junction

Typ III: Distal of the cardia, out of intestinal metaplasia of the esophagogastric junction or dysplasia of stomach

Classification by Histology

WHO histological classification of gastric tumours

Lauren classification

Classification by Histology

WHO histological classification of gastric tumours

Epithelial tumours

Intraepithelial neoplasia – Adenoma

Carcinoma

- Adenocarcinoma
  - intestinal type
  - diffuse type

>90%

- Papillary adenocarcinoma
- Tubular adenocarcinoma
- Mucinous adenocarcinoma
- Signet-ring cell carcinoma
- Adenosquamous carcinoma
- Squamous cell carcinoma
- Small cell carcinoma
- Undifferentiated carcinoma
- Others

Carcinoid (well differentiated endocrine neoplasm)

Non-epithelial tumours

- Leiomyoma
- Schwannoma
- Granular cell tumour
- Glomus tumour
- Leiomyosarcoma
- GI stromal tumour
  - benign
  - uncertain malignant potential
  - malignant
- Kaposi sarcoma
- Others

Malignant lymphomas

- Marginal zone B-cell lymphoma of MALT-type
- Mantle cell lymphoma
- Diffuse large B-cell lymphoma
- Others

Secondary tumours

Lauren classification

Classification by Histology

WHO histological classification of gastric tumours

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Lauren classification

	Intestinal	Diffuse
Morphology	**Glandular** structure	**Poorly cohesive**, or dispersed single cells
Frequent sites of metastasis	Liver	Ovary, Peritoneum
Other remarks	Associated with atrophic gastritis, intestinal metaplasia	Familial variant involving ***CDH1*** germline mutation
HER2	Higher	Lower

Staging

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CT Thorax/Abdomen
- Sensitivity for metastasis around 70%!

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PET/CT
- Low detection rate in diffuse and mucinous tumor types (low tracer accumulation)

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Explorative laparoscopy
- To roule out M+ carcinosis- with cytology
- Indicated for clinical stage T1b or higher (especially for diffuse type)
- In 13-57% detection of metastasis not seen in CT

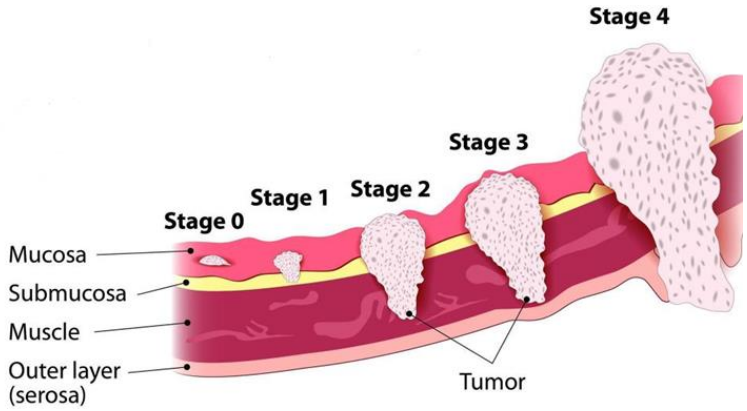
Staging EUS

Operator depending
46-88% for T-Staging (often overstaged)
30-90% for N-staging
Detection of Ascites in 8% with normal CT

T1
Mucosa(T1a)
Submucosa (T1b)

T2 Muscularis propria

T3 Subserosa



T4 Perforation of the serosa,
T4a through the outer lining of the stomach wall
T4b involving other organs

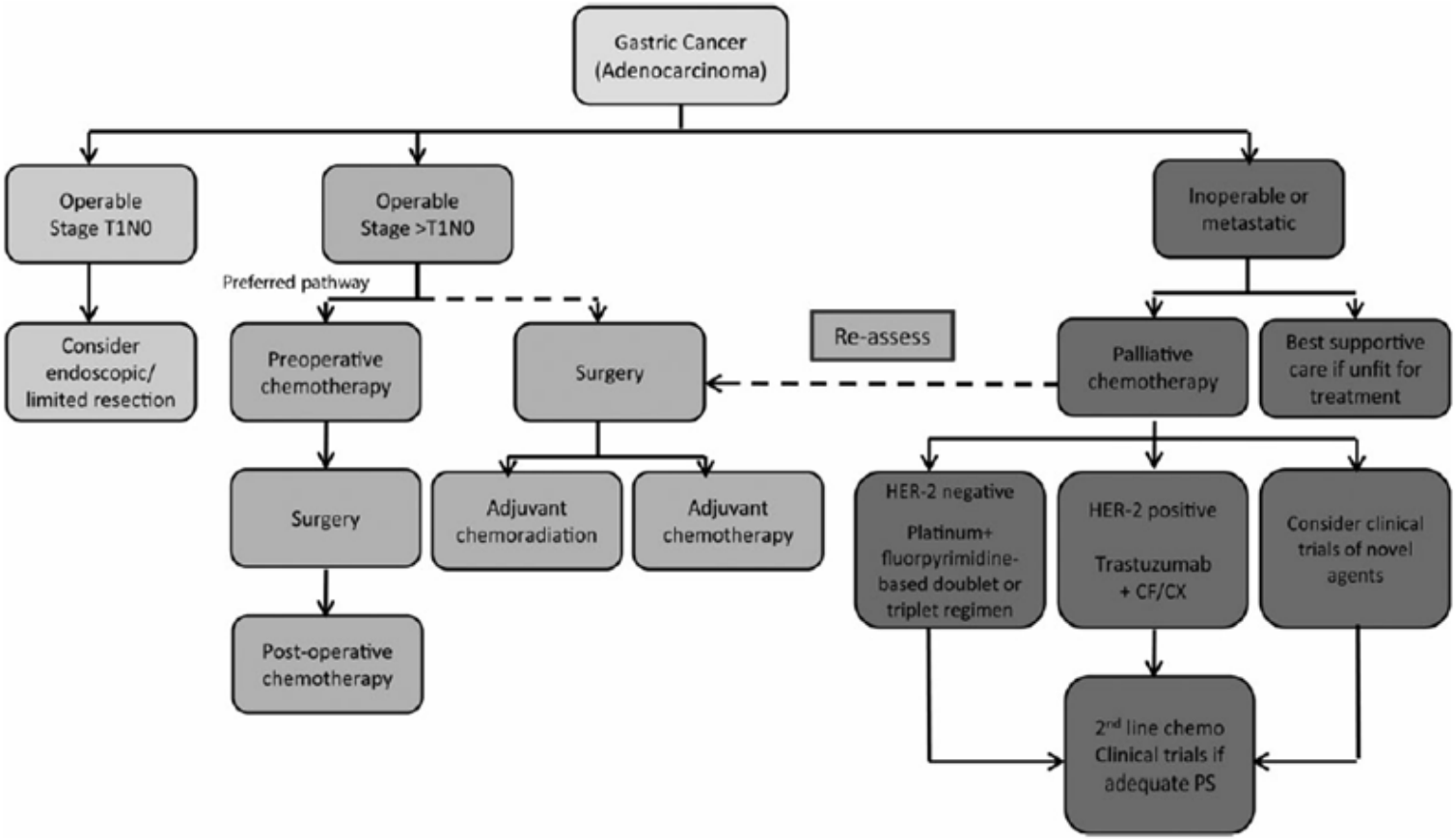
When EMR/ESD/Surgery ?

When EMR/ESD/Surgery ?

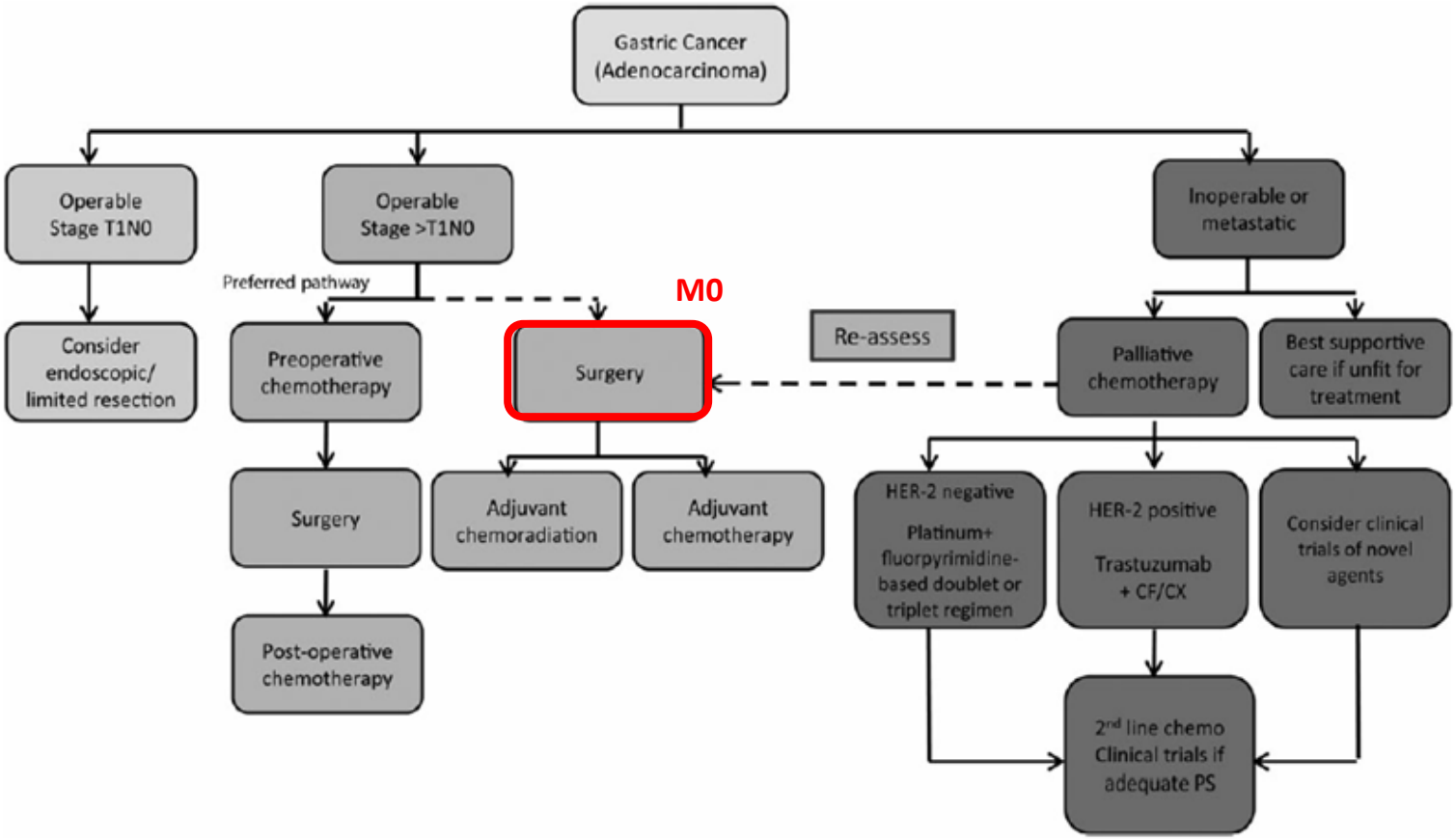
Criteria for curative endoscopic resection in early gastric cancer

	Mucosal cancer				Submucosal cancer	
	No ulcer		Ulcer present		Sm1 (<500 um)	Sm2 (>500 um)
Size (mm)	< 20	> 20	< 30	> 30	< 30	Any size
Differen-tiated cancer	EMR	ESD	ESD	Surgery	ESD	Surgery
Undiffe-rentiated cancer	Surgery considered	Surgery	Surgery	Surgery	Surgery	Surgery

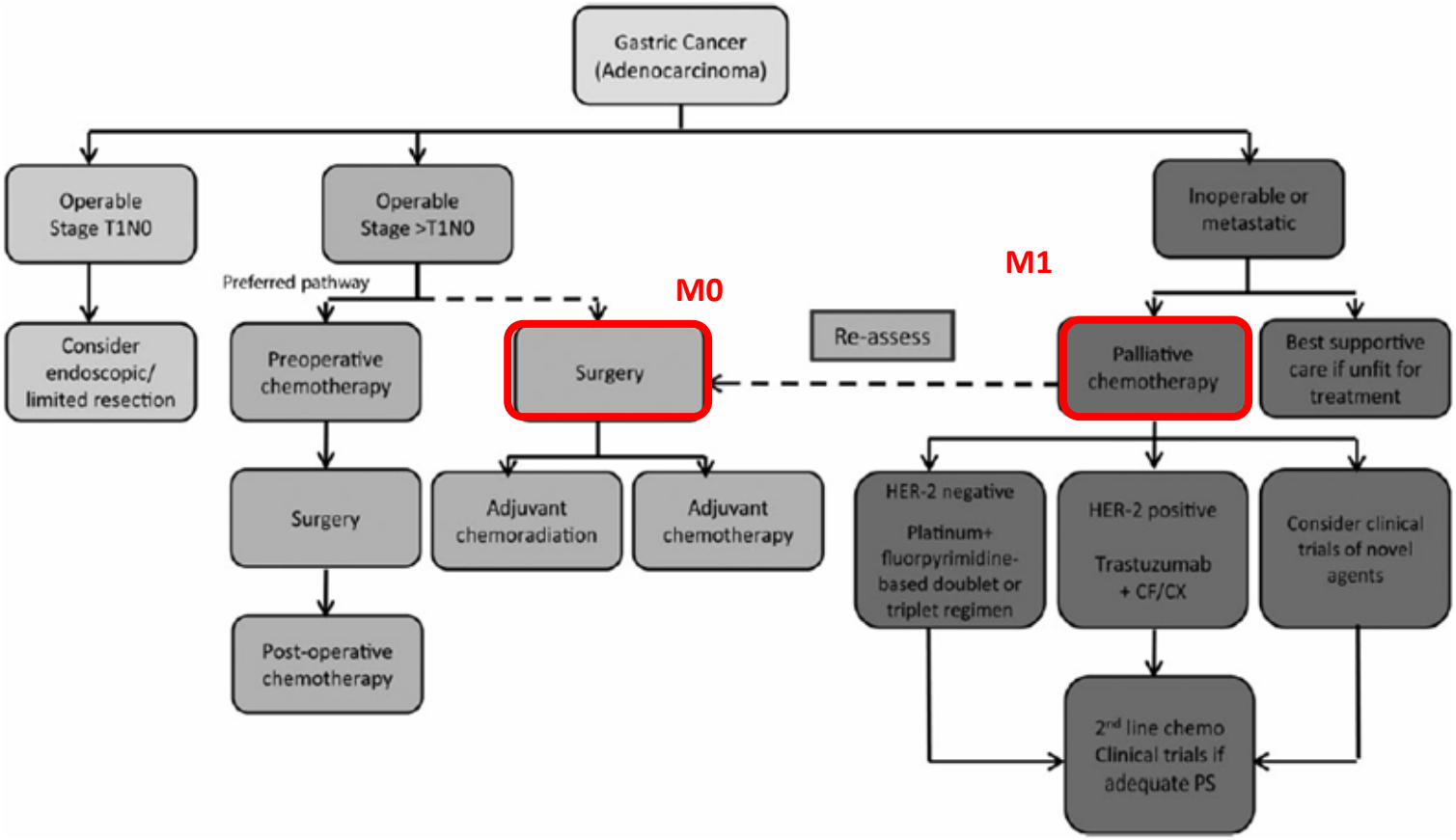
Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer-Digestive Endoscopy 2016; 28: 3–15



Waddell T. Ann Oncol. 2013 Oct;24 Suppl 6:vi57-63.



Waddell T. Ann Oncol. 2013 Oct;24 Suppl 6:vi57-63.

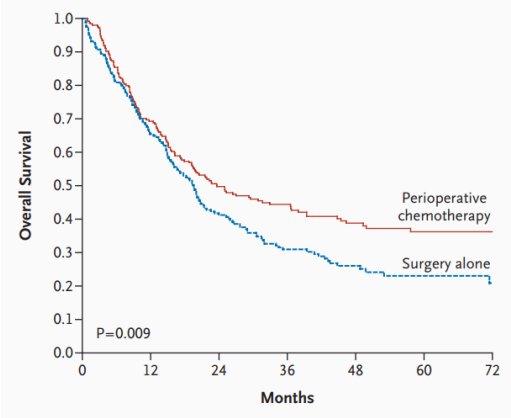


Waddell T. Ann Oncol. 2013 Oct;24 Suppl 6:vi57-63.

Chemotherapy

Perioperativ – standad Cunningham et al, 2007

- Platinum/Fluoropyrimidine
- 5 year survival 36% with chemotherapy vs. 23%



Palliativ - bei M1 (UICC IV) Wagner et al, 2017

- Chemotherapy +6.7 Months compared with best supportive care

Moehler M. Z Gastroenterol. 2011;49(4).

Cunningham D. N Engl J Med. 2006 Jul 6;355(1):11-20.

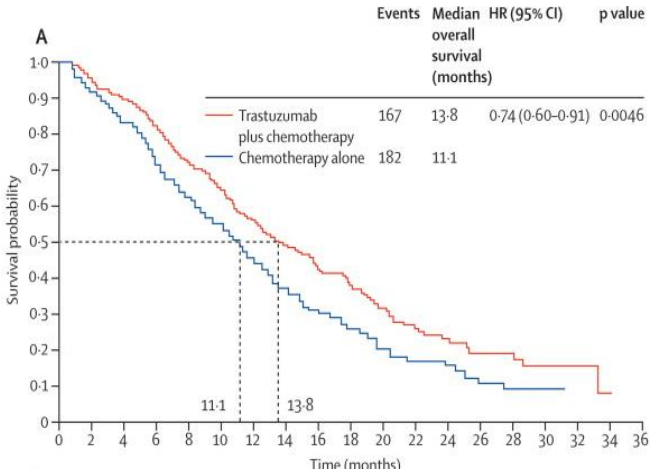
Wagner AD. Cochrane Database Syst Rev. 2017 Aug 29;8:CD004064

Targeted Therapy HER2

22% of all castric cancers are HER2+
Trastuzumab (Herceptin®) licensed since 2010

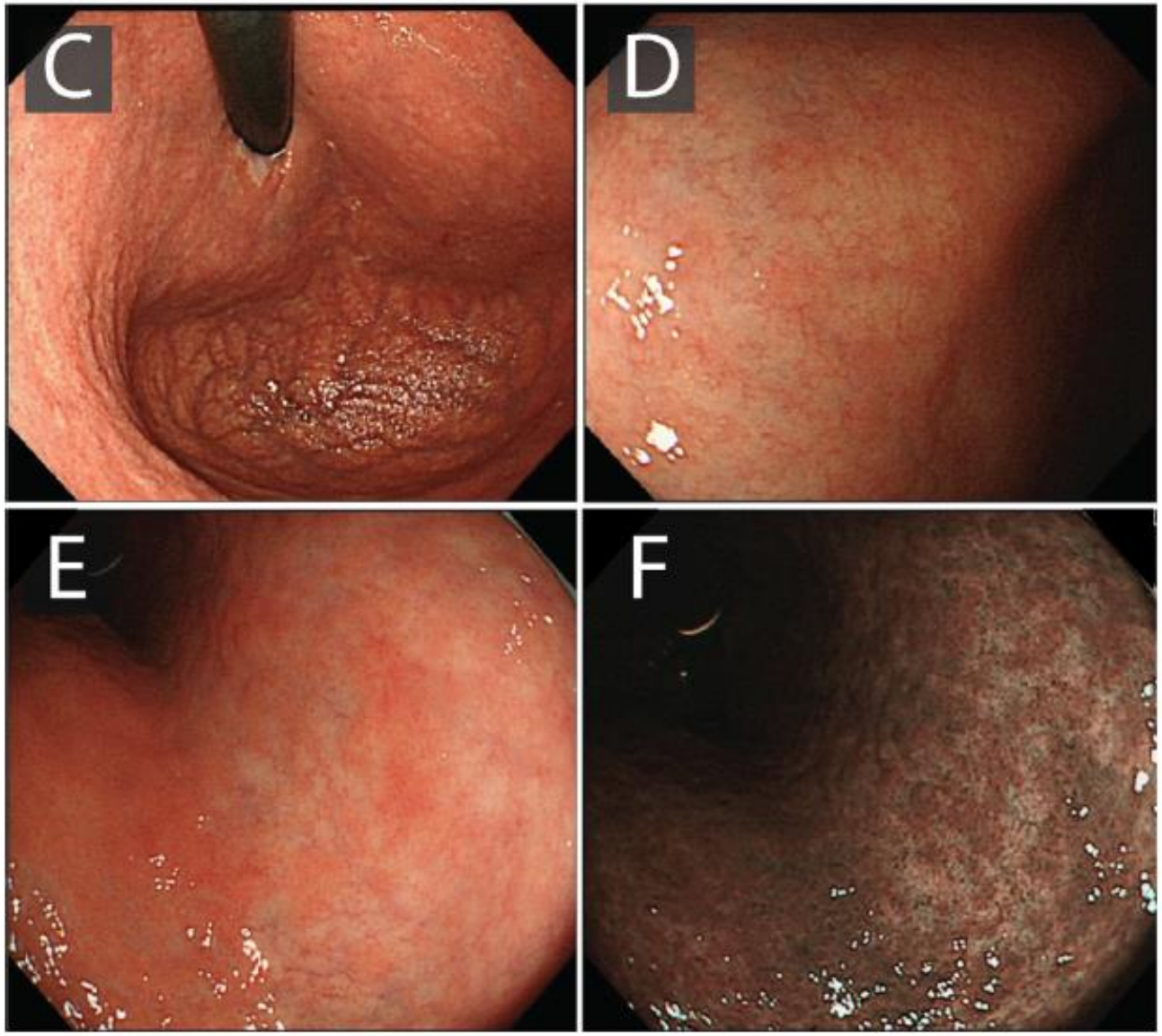
- Median survival withTrastuzumab:
  - 13.8 Months vs. Chemotherapy alone 11.1 Months

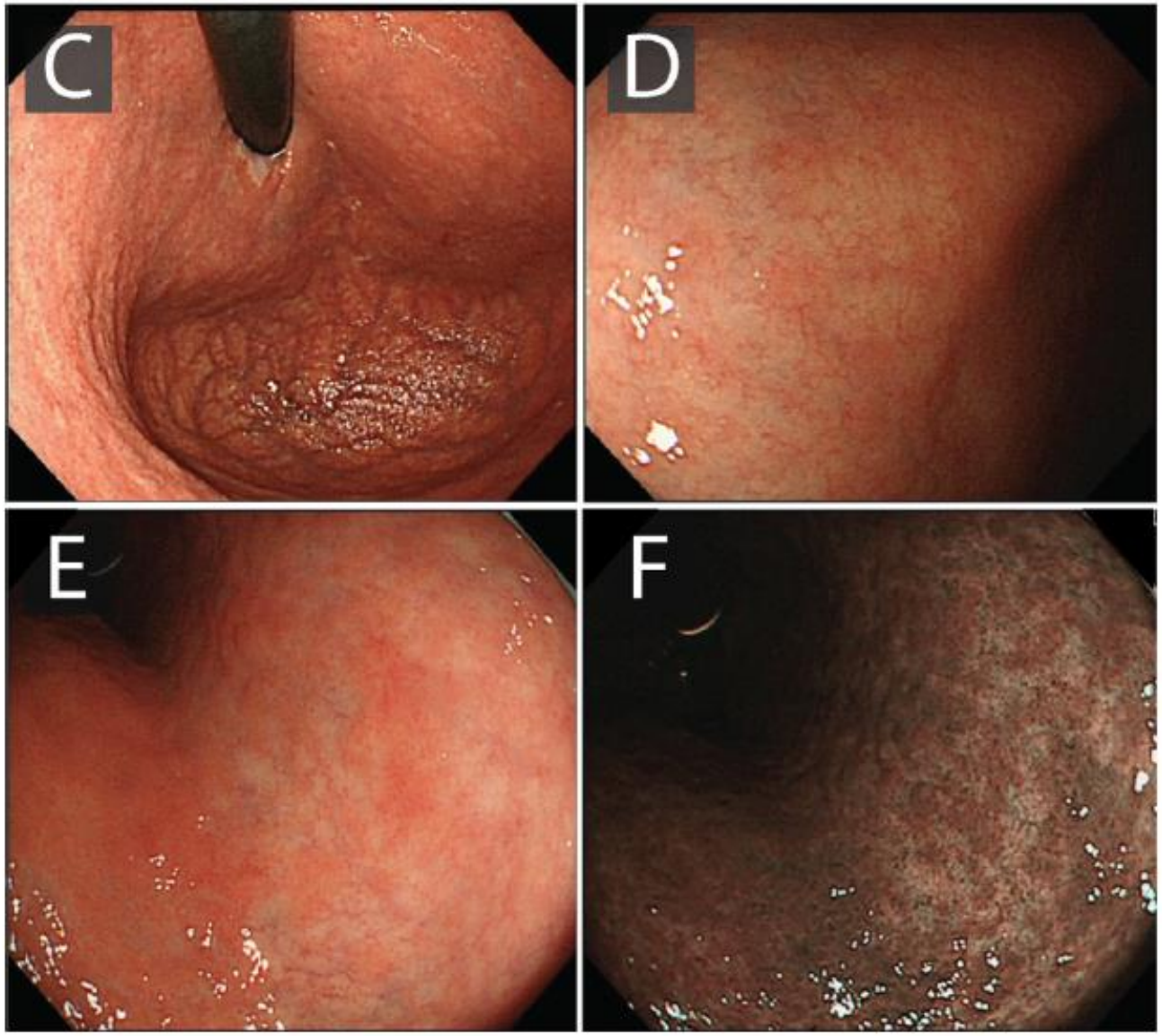
- No more side effects



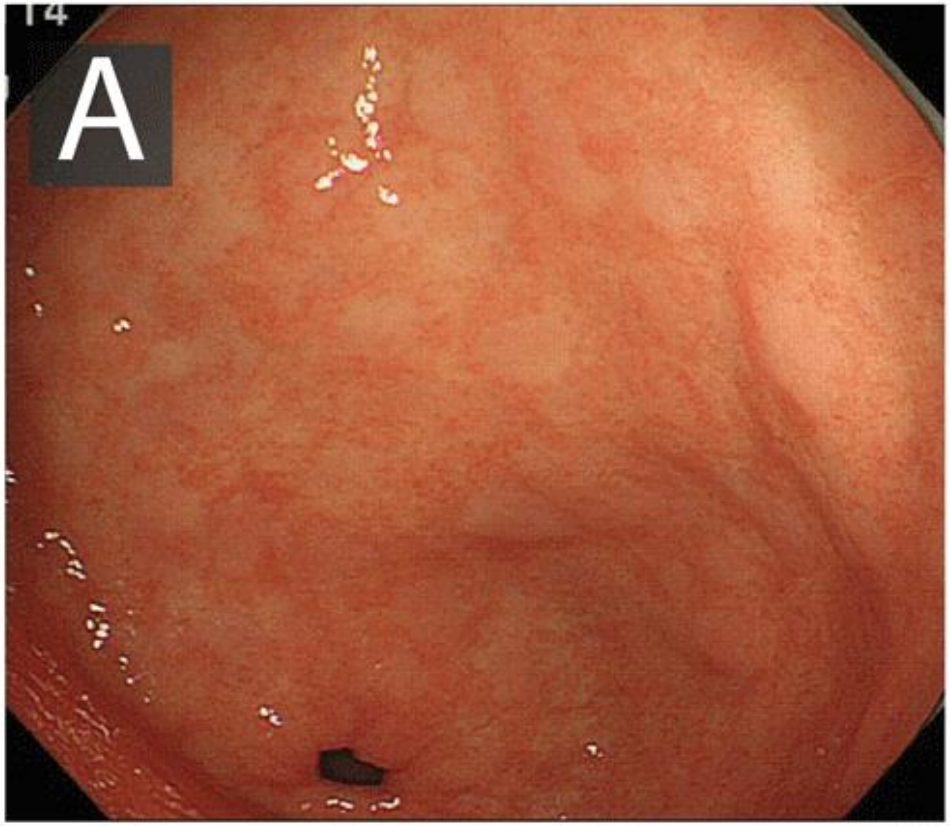
Bang et al, 2010:
ToGA-Trial (Trastuzumab for Gastric Cancer): RCT, 122 Zentren, 584 **inoperable** Patienten:
Chemotherapie vs Trastuzumab + Chemotherapie
(Capecitabine/5-FU + Cisplatin je 6x3Wo)

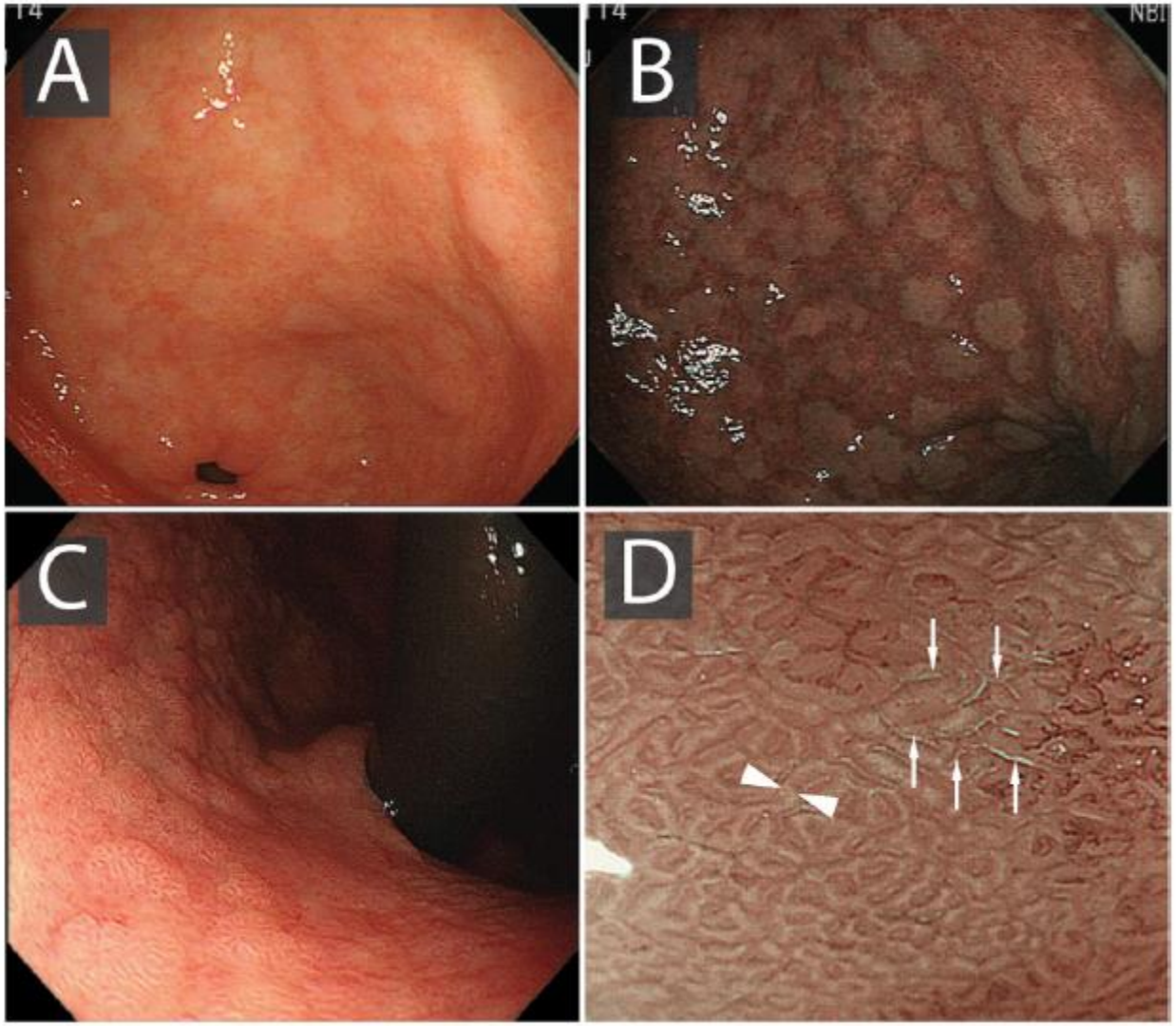
Quiz

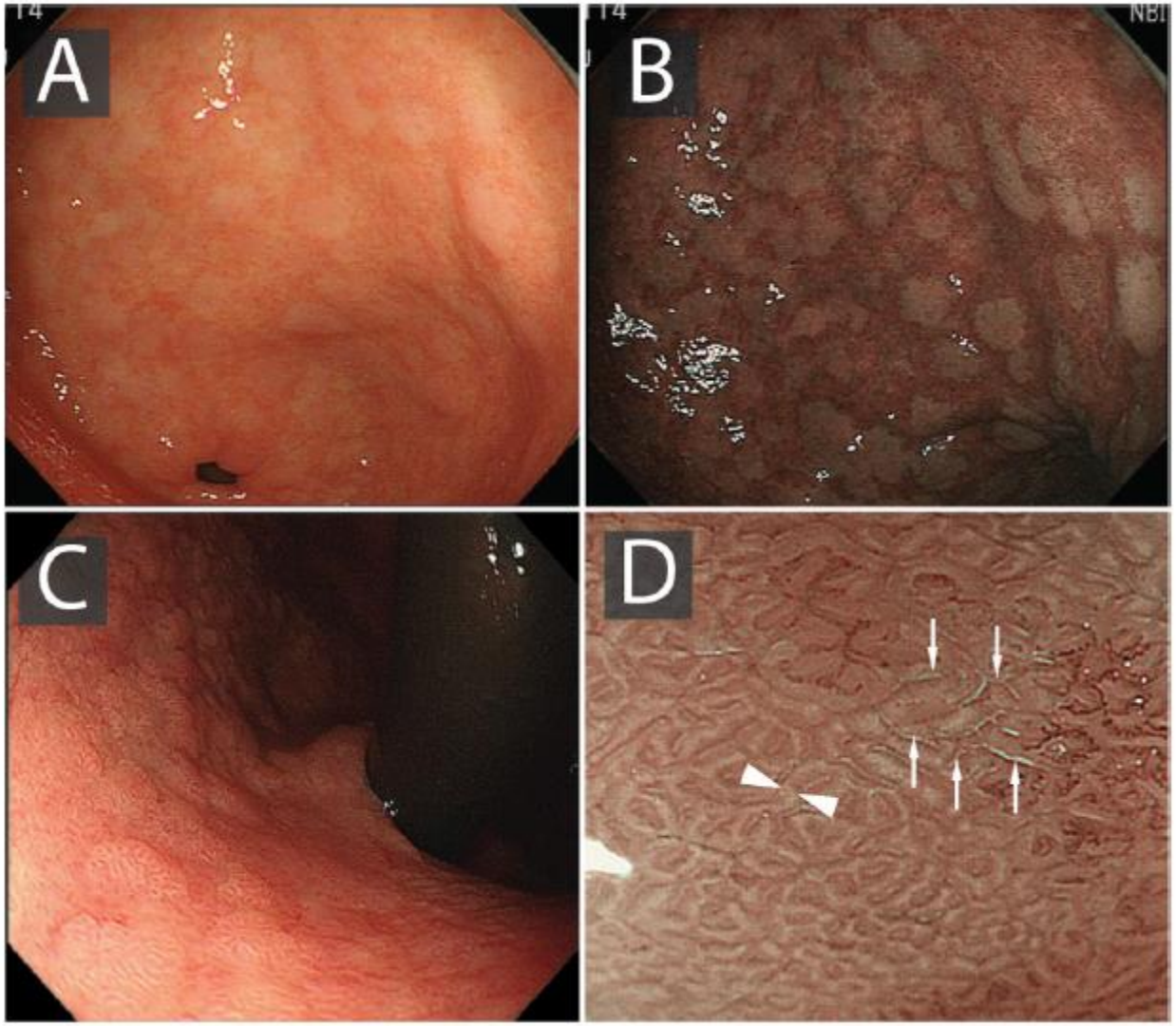

C
D
E
F



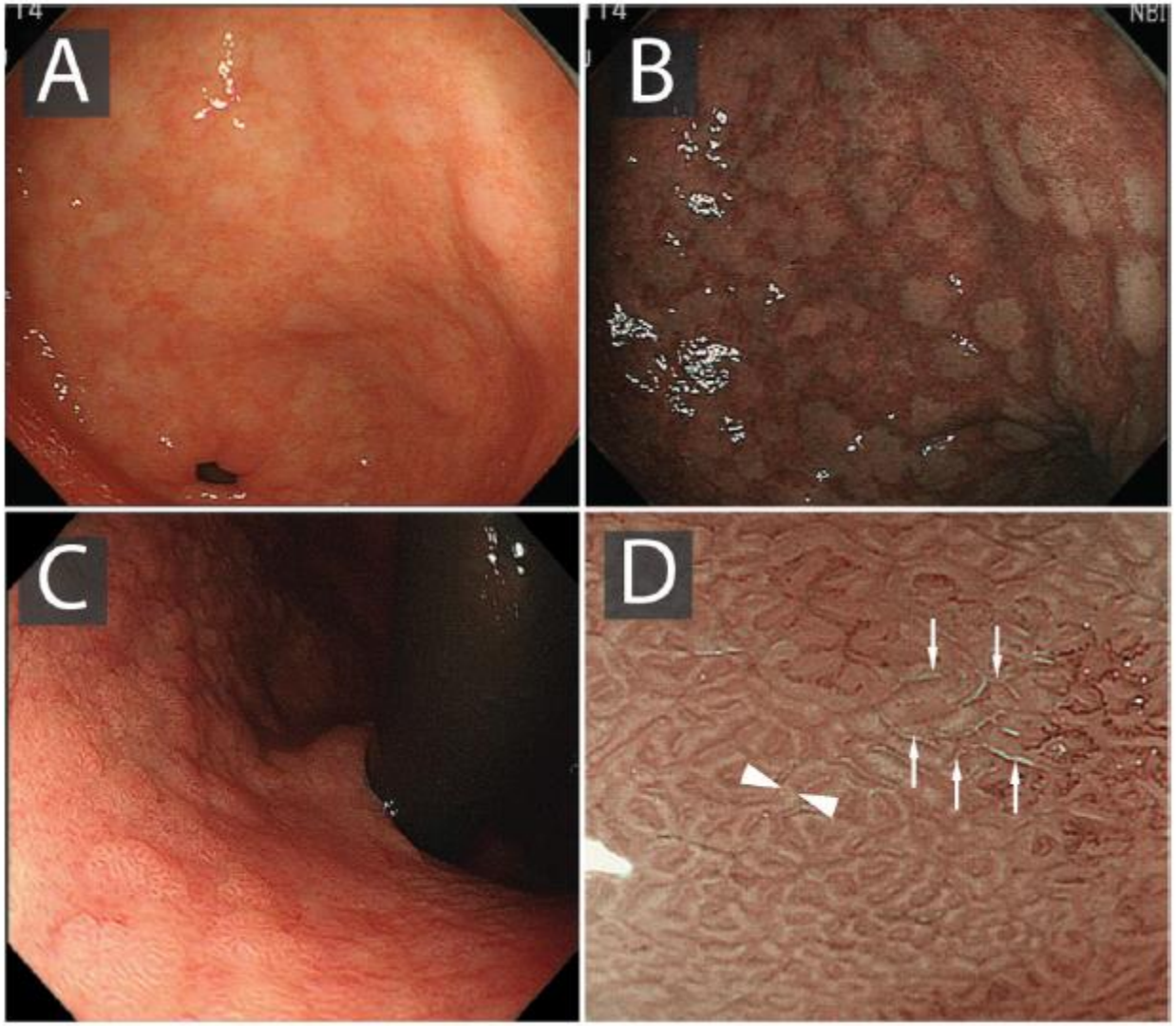
Chronic atrophic gastritis


A


A
B
NBI
C
D



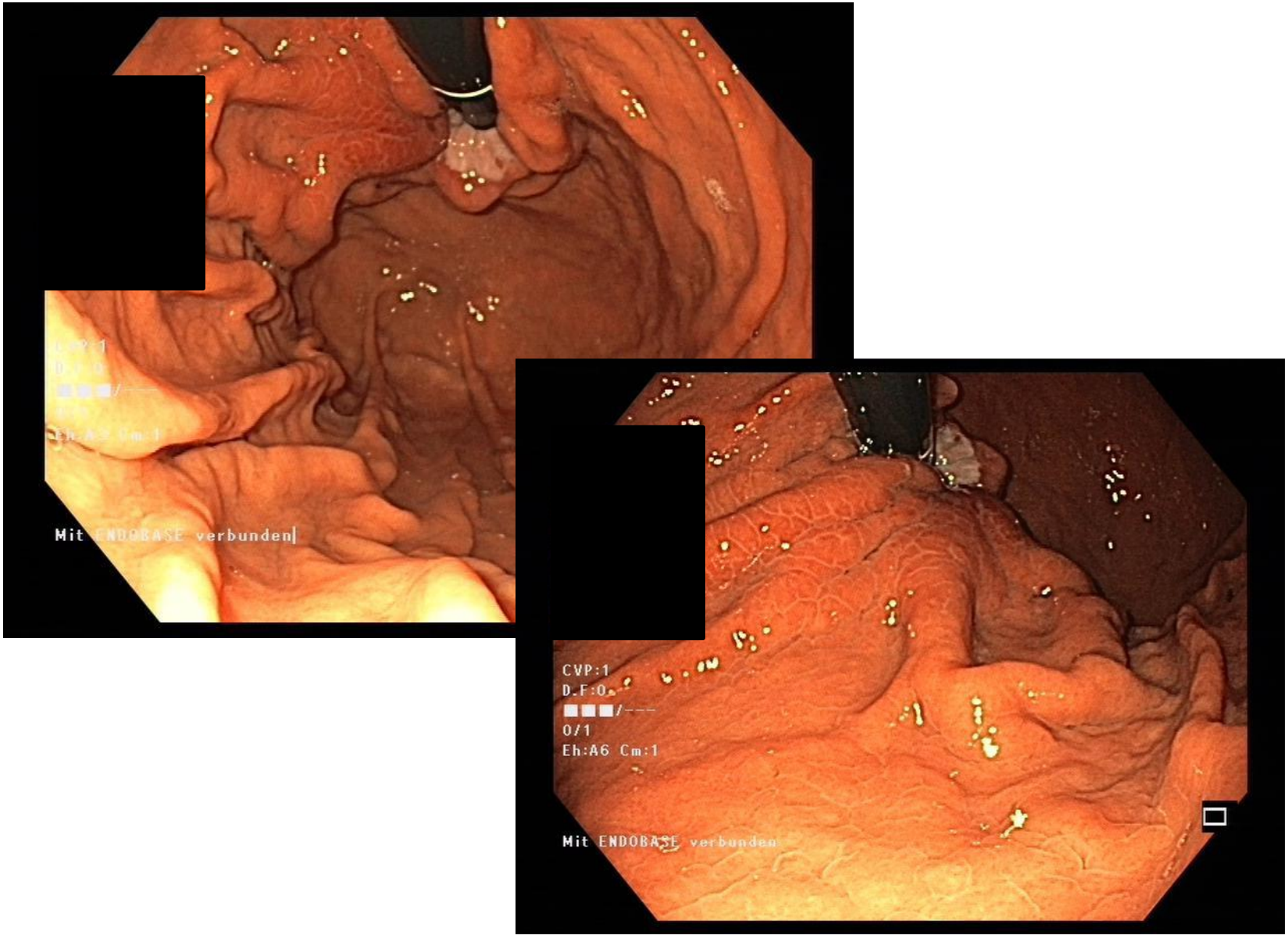
light blue crest (LBC)

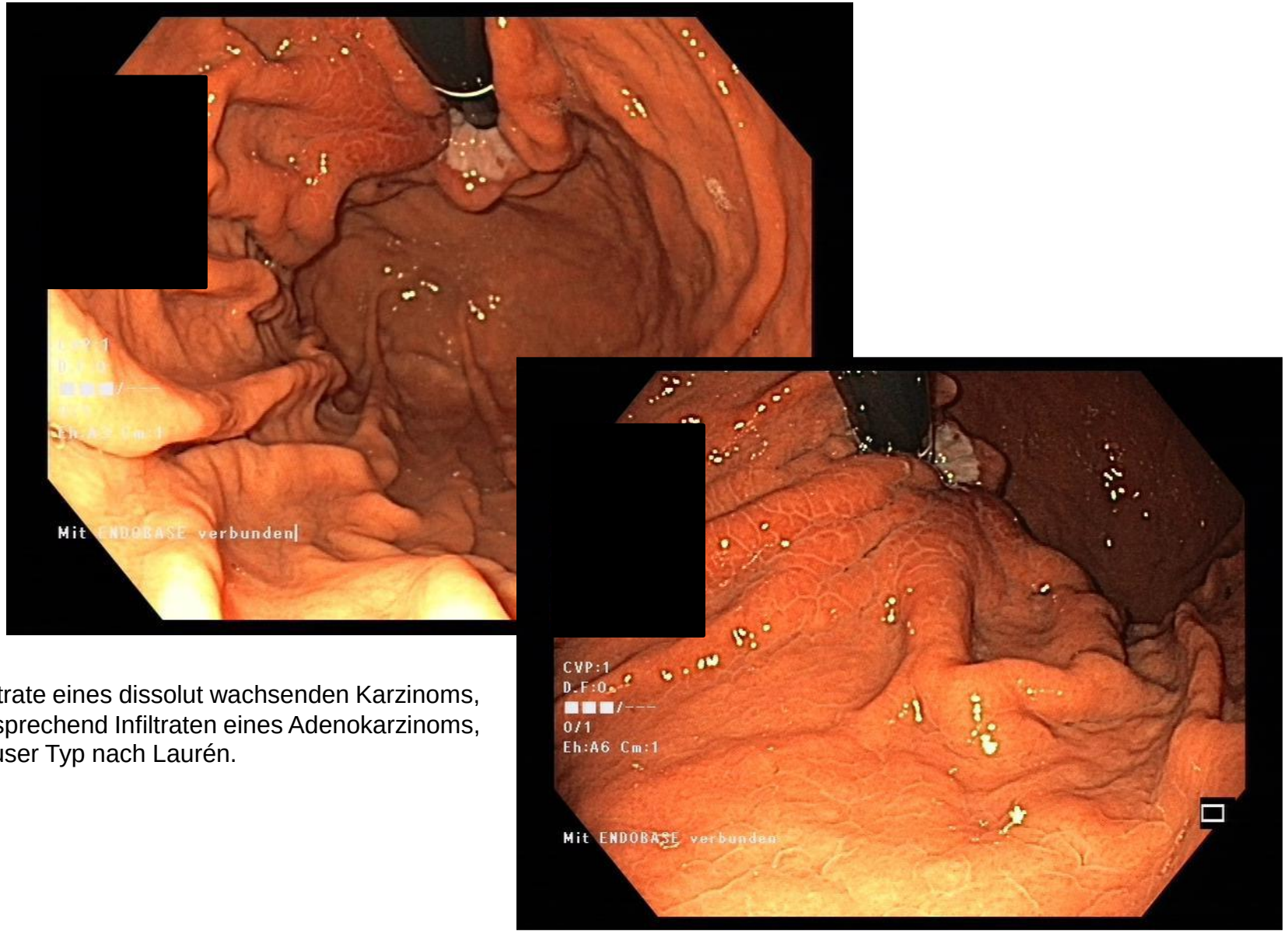


light blue crest (LBC)

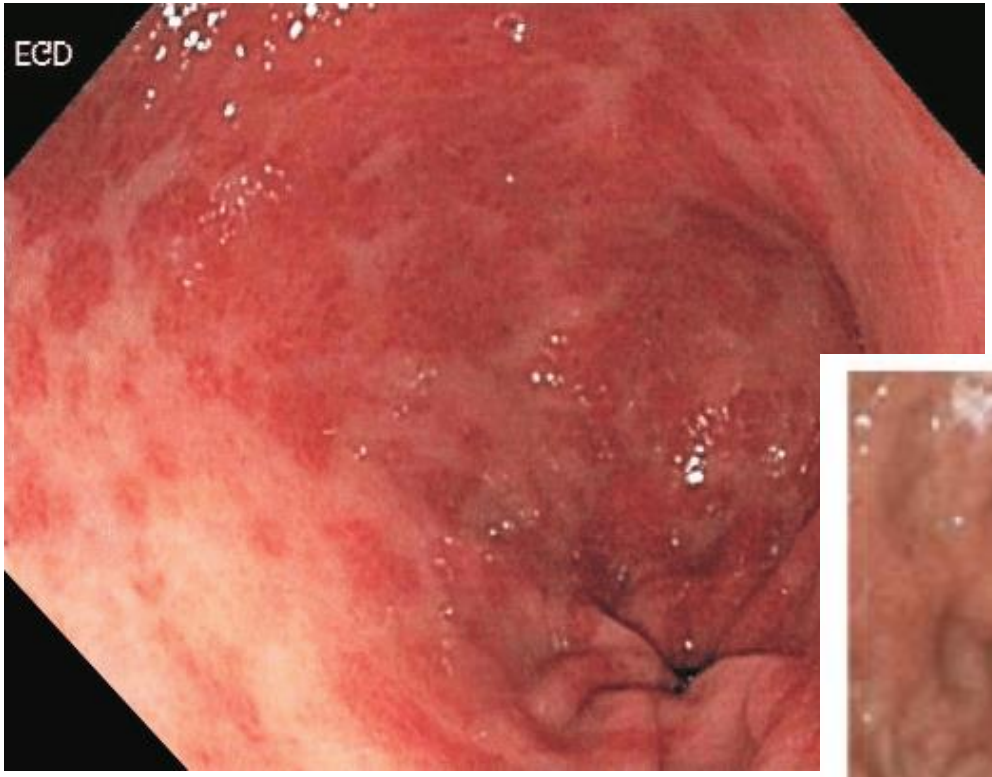
marginal turbid band (MTB)

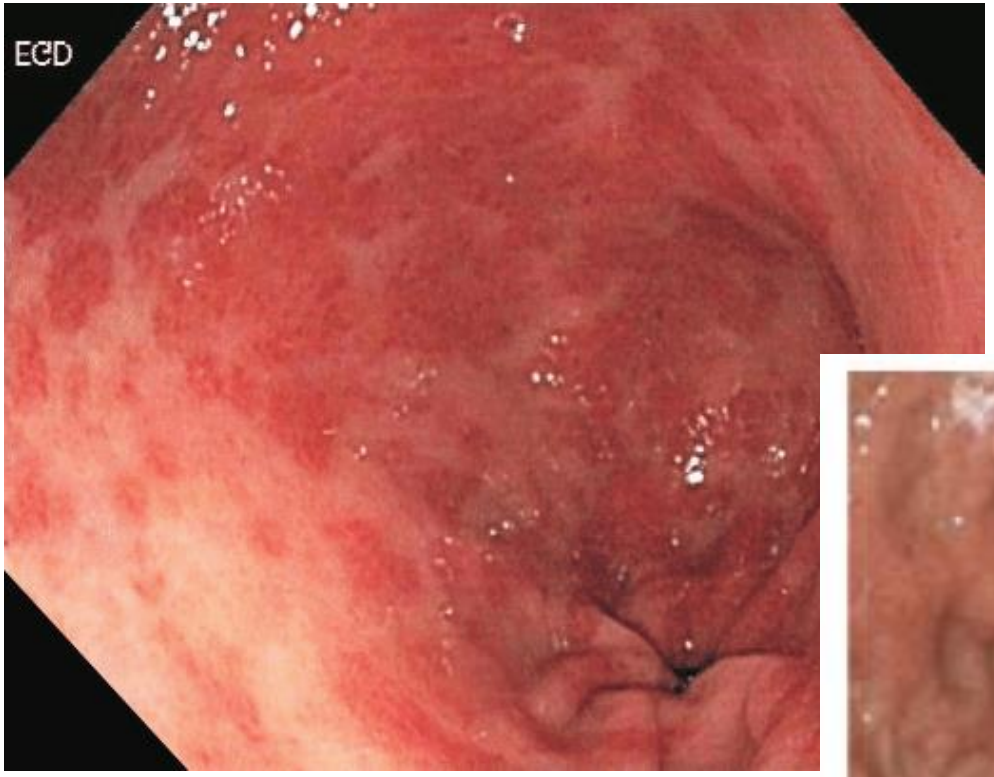
Portal hypertensiv gastropathy


CVP:1
D.F:O
O/1
Eh:A6 Cm:1
Mit ENDOBASE verbunden

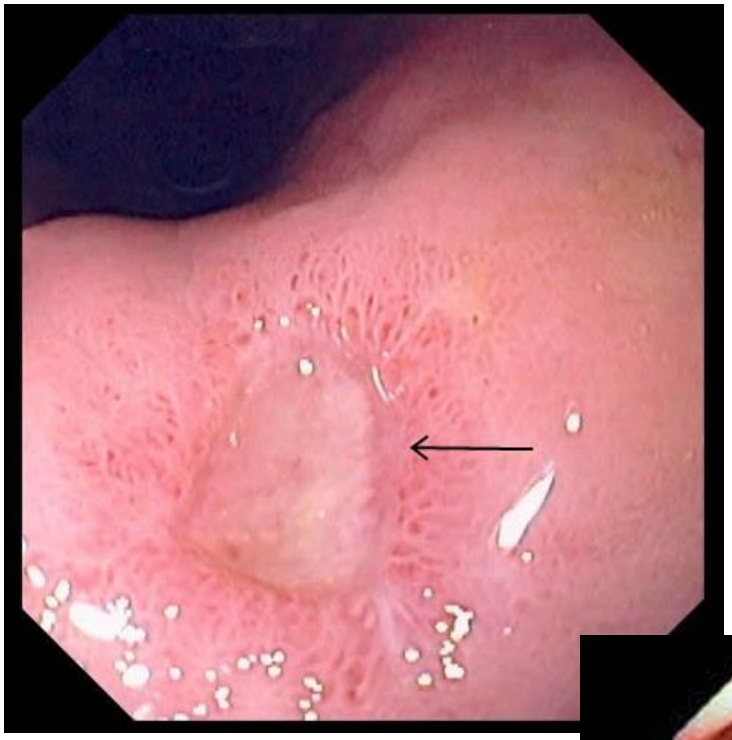


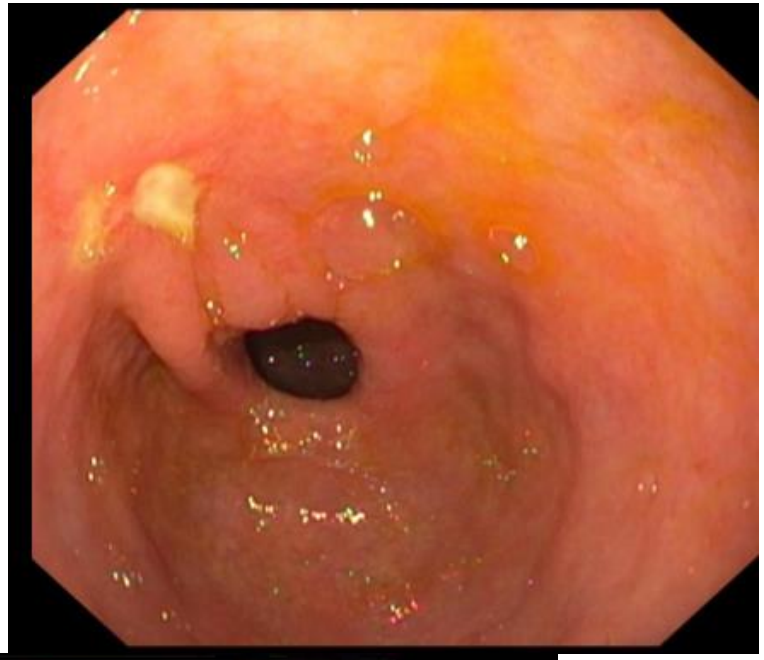
Infiltrate eines dissolut wachsenden Karzinoms, entsprechend Infiltraten eines Adenokarzinoms, diffuser Typ nach Laurén.

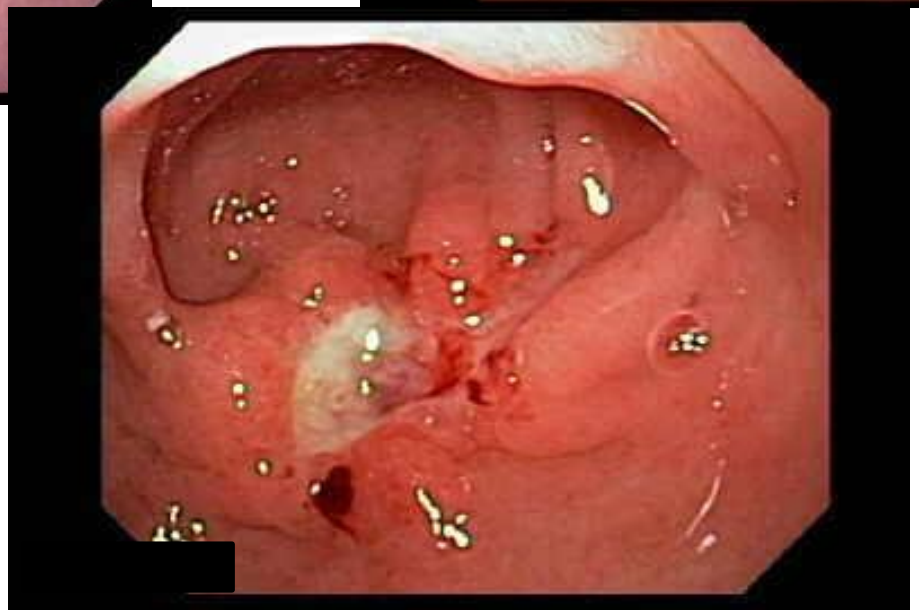

ECD

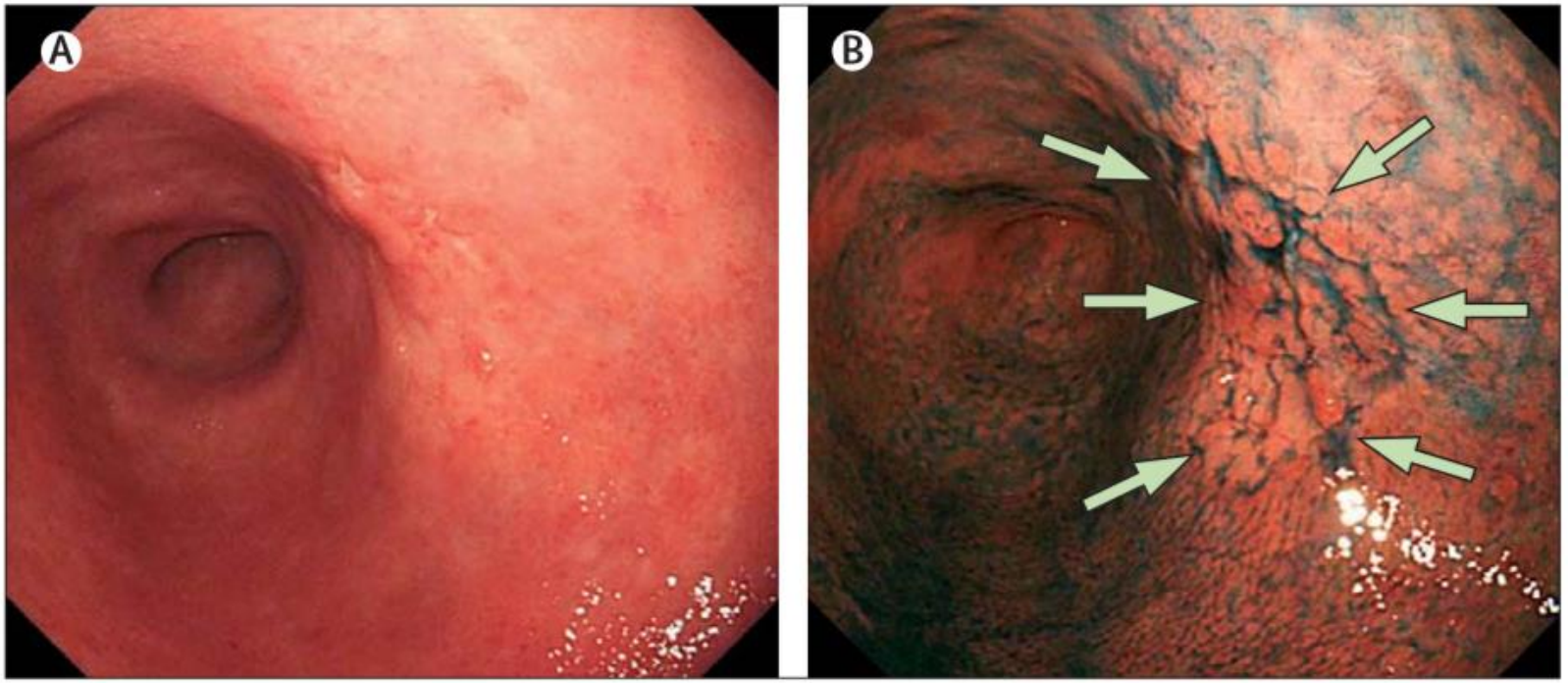


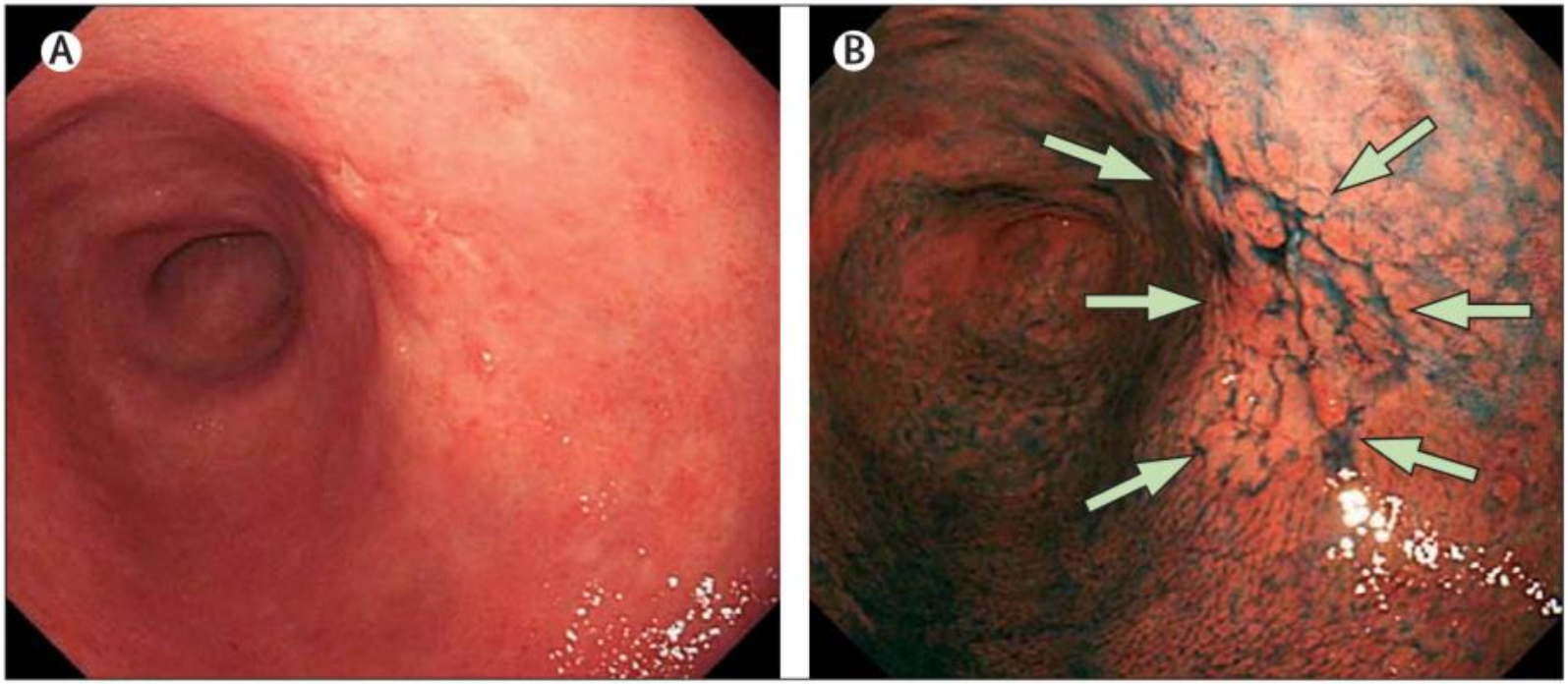
Linitis plastica
(type of adenocarcinoma) spreads to the muscles of the stomach wall and makes it thicker and more rigid.








A
B



Adenocarcinoma

Questions?