

BILIARY TRACT CANCERS

A- Gall Bladder Cancer

Initial Workup

- History and examination
- CT or MRI
- Chest imaging
- LFT
- CEA
- Ca 19-9

TNM Staging

Tumor	
T	Primary Tumor
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor invades lamina propria or muscular layer
T1a	Tumor invades lamina propria
T1b	Tumor invades muscular layer
T2	Tumor invades perimuscular connective tissue; no extension beyond serosa or into the liver.
T2a	Tumor invades perimuscular connective tissue on the peritoneal surface without the involvement of the serosa.
T2b	Tumor invades perimuscular connective tissue on the hepatic side with no extension into the liver.
T3	Tumor perforates: <ul style="list-style-type: none"> • The serosa (visceral peritoneum) and/or • Directly invades the liver and/or • One other adjacent organ or structure, such as the stomach, duodenum, colon, pancreas, omentum or extrahepatic bile ducts.
T4	Tumor invades main portal vein or hepatic artery or invades two or more extrahepatic organs or structures.

Node Status	
N	Regional Lymph Nodes
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis in one to three regional lymph nodes
N2	Metastasis in four or more regional lymph nodes

Metastasis	
M	Distant Metastasis
M0	No distant metastases
M1	Distant metastasis

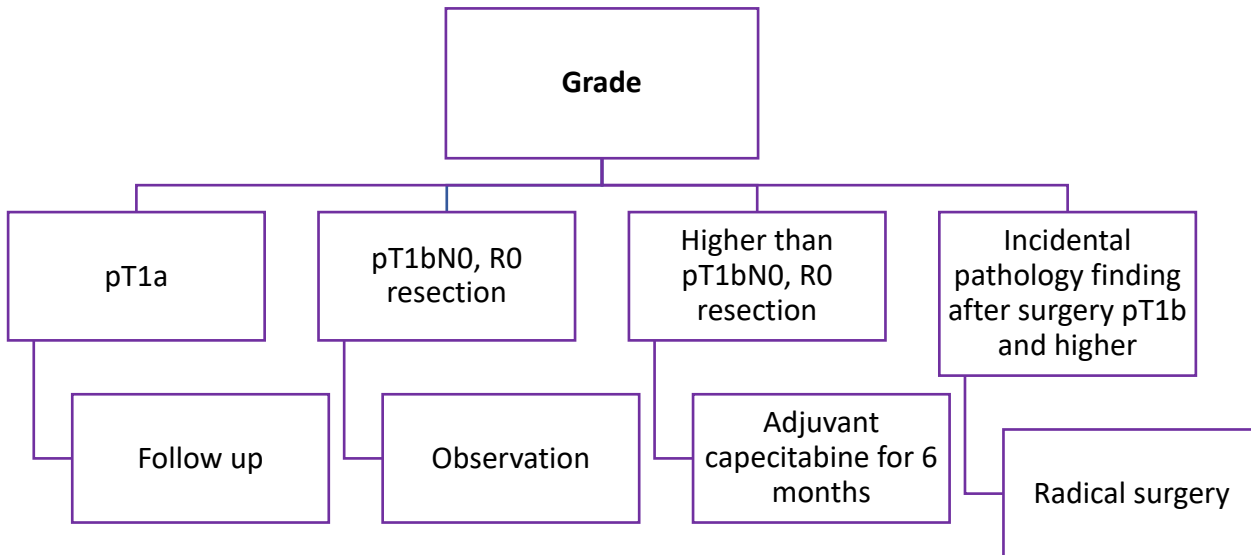
Histologic Grading	
Gx	The grade cannot be assessed
G1	Well-differentiated
G2	Moderately differentiated
G3	Poorly differentiated

Stage Grouping			
	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T1, T2, T3	N1	M0
Stage IVA	T4	N0, N1	M0
Stage IVB	Any T	N2	M0
	Any T	Any N	M1

A- Resectable Tumor

Treatment:

- Cholecystectomy +
- En bloc hepatic resection +
- Lymphadenectomy with or without bile duct resection.



Surveillance:

- There are no data to support an aggressive follow-up.
- Imaging studies every 6 months is an acceptable approach.

B- Unresectable (Locally Advanced)

- Gemcitabine/Cisplatin-based combination therapy
- Other Gemcitabine-based or Fluoropyrimidine-based chemotherapy
- EBRT with concurrent fluoropyrimidine
- Radiation Therapy
- Pembrolizumab (Only MSI-H/dMMR tumors)
- Supportive care for the patient who can't tolerate chemotherapy.

C- Metastatic or Recurrent Gallbladder Cancer

- Gemcitabine/Cisplatin-based chemotherapy
- Other Gemcitabine or Fluoropyrimidine-based chemotherapy
- Pembrolizumab (if MSI H/dMMR tumors)
- Best supportive care

B- Intrahepatic Cholangiocarcinoma

Initial Workup

- History and examination
- Full radiological staging by CT or MRI
- Lab: LFT, CEA and Ca 19-9
- May consider laparoscopy

TNM Staging

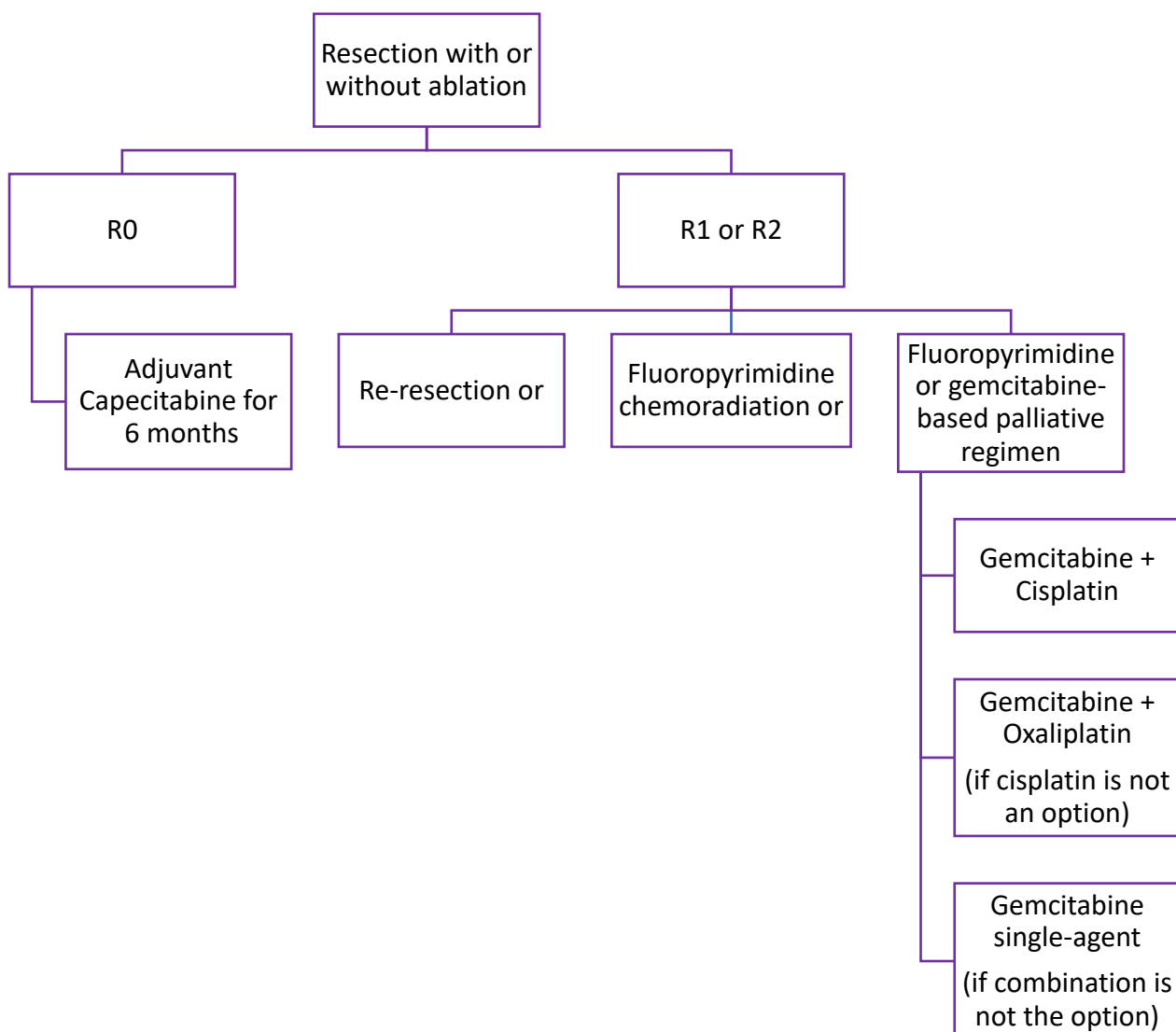
Tumor	
T	Primary Tumor
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ (intraductal tumor)
T1	Solitary tumor without vascular invasion < 5cm or > 5cm
T1a	Solitary tumor < 5cm without vascular invasion
T1b	Solitary tumor > 5 cm without vascular invasion
T2	Solitary tumor with intrahepatic vascular invasion or multiple tumors with or without vascular invasion
T3	Tumor perforating the visceral peritoneum
T4	Tumor involving the local extrahepatic structures by direct invasion

Node Status	
N	Regional Lymph Nodes
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Regional lymph node metastasis present

Metastasis	
M	Distant Metastasis
M0	No distant metastases
M1	Distant metastasis present

Histological Grade	
Gx	The grade cannot be assessed
G1	Well-differentiated
G2	Moderately differentiated
G3	Poorly differentiated

Stage Grouping			
	T	N	M
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

A. Resectable Tumor**B. Unresectable (Locally Advanced):**

- Gemcitabine/Cisplatin-based combination therapy
- Other Gemcitabine-based or Fluoropyrimidine-based chemotherapy
- EBRT with concurrent Fluoropyrimidine
- Radiation Therapy
- Arterial directed therapy
- Pembrolizumab (only MSI-H/dMMR tumors)
- Supportive care for the patient who cannot tolerate chemotherapy.

C. Metastatic or Recurrent Disease:

- Gemcitabine/Cisplatin-based combination therapy
- Fluoropyrimidine-based or other Gemcitabine-based chemotherapy
- EBRT with concurrent Fluoropyrimidine
- Radiation Therapy
- Arterial directed therapy
- Pembrolizumab (only MSI-H/dMMR tumors)
- Supportive care for the patient who cannot tolerate chemotherapy.

Surveillance:

- There are no data to support an aggressive follow-up.
- Imaging studies every 6 months is an acceptable approach.
- Patients on palliative chemotherapy:
 - CT Scan every 3-4 months to evaluate the response.

C- Extrahepatic Cholangiocarcinoma**Initial Workup**

- History and examination
- CT or MRI
- MRCP
- Chest imaging
- Endoscopic ultrasound
- LFT
- CEA
- Ca 19-9

The TNM staging of perihilar cholangiocarcinoma

Tumor	
T	Primary Tumor
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor confined to the bile duct, with extension up to the muscle layer or fibrous tissue
T2a	Tumor invades beyond the wall of the bile duct to surrounding adipose tissue

T2b	Tumor invades adjacent hepatic parenchyma
T3	Tumor invades unilateral branches of the portal vein or hepatic artery
T4	Tumor invades: The main portal vein or its branches bilaterally or The common hepatic artery or The second-order biliary radicals bilaterally or Unilateral second-order biliary radicals with contralateral portal vein or Hepatic artery involvement

Nodal Status

N	Regional Lymph Nodes
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	< Four positive lymph nodes typically involving the hilar, cystic duct, common bile duct, hepatic artery, posterior pancreaticoduodenal, and portal vein lymph nodes
N2	≥ Four positive lymph nodes from the sites described for N1

Metastasis

M	Distant Metastasis
M0	No distant metastases
M1	Distant metastasis present

Histological Grade

Gx	The grade cannot be assessed
G1	Well-differentiated
G2	Moderately differentiated
G3	Poorly differentiated

Stage grouping			
	T	N	M
Stage 0	Tis	N0	M0
Stage I	T	N0	M0
Stage II	T2a, T2b	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T1–3	N1	M0
Stage IVA	T4	N0–1	M0
Stage IVB	Any T	N2	M0
	Any T	Any N	M1

The TNM staging of distal bile duct tumors

Table (1)	
T	Primary Tumor
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor confined to the bile duct with a depth < 5mm
T2	Tumor invades the bile duct wall with a depth of 5-12 mm
T3	Tumor invades the bile duct wall with a depth greater than 12 mm
T4	Tumor involves the celiac axis, superior mesenteric artery, and or common hepatic artery

Table (2)	
N	Regional Lymph Nodes
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis to one to three regional nodes
N2	Metastasis in four or more regional nodes

Table (3)

M	Distant Metastasis
M0	No distant metastases
M1	Distant metastasis present

Histological Grade

Gx	Grade cannot be assessed
G1	Well-differentiated
G2	Moderately differentiated
G3	Poorly differentiated

Stage Grouping

	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0–1	M0
Stage IIIA	T1–3	N2	M0
Stage IIIB	T4	N0–2	M0
Stage IV	Any T	Any N	M1

Resected, R0, and Negative Nodes:

Adjuvant capecitabine for 6 months

Resected, R1, or Positive LNs:

- Fluoropyrimidine-based or Gemcitabine/cisplatin-based combination therapy
- EBRT with concurrent Fluoropyrimidine.
- Fluoropyrimidine-based or Gemcitabine-based chemotherapy, followed by Fluoropyrimidine-based chemoradiation.

- Fluoropyrimidine-based chemoradiation followed by Fluoropyrimidine-based or Gemcitabine-based chemotherapy.

Resected, R2:

Gemcitabine/Cisplatin-based combination therapy

EBRT with concurrent Fluoropyrimidine.

Fluoropyrimidine-based or Gemcitabine-based chemotherapy

Radiation Therapy

Pembrolizumab (only for MSI-H/dMMR tumors)

Best supportive care

Metastatic or Recurrent Disease:

- Gemcitabine /cisplatin-based chemotherapy
- Fluoropyrimidine-based or other Gemcitabine-based combination chemotherapy
- Pembrolizumab (only for MSI H/dMMR tumors)
- Best supportive care

Surveillance:

- There are no data to support an aggressive follow-up.
- Imaging studies every 6 months is an acceptable approach.
- Patients on palliative chemotherapy:
- CT scan every 3-4 months to evaluate the response.

Chemotherapy Regimes**Single-agent Gemcitabine**

Gemcitabine	1000 mg/m ² IV on days 1, 8 and 15
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Repeated every 4 weeks

Gemcitabine + Oxaliplatin

Gemcitabine	1000 mg/m ² on day 1
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Oxaliplatin	85 mg/m ² on day 1
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Repeat every 2 weeks

Gemcitabine + Cisplatin

Gemcitabine	1000 mg/m ² on days 1 and 8
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Cisplatin	75 mg/m ² on days 1
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Repeat every 3 weeks

Capecitabine

Capecitabine	1000 mg/m ² /day B.D. for 14 days
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Repeated every 3 weeks

Capecitabine + Oxaliplatin

Capecitabine	1000 mg/m ² /day B.D. for 14 days
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Oxaliplatin	130 mg/m ²
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Repeat every 3 weeks

Capecitabine + Oxaliplatin

Capecitabine	800 mg/m ² /day B.D. for 9 days
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Oxaliplatin	85 mg/m ²
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Repeat every 2 weeks

Pembrolizumab

Pembrolizumab	200 mg
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Repeated every 3 weeks