

GALL BLADDER CANCER

BASIC WORK UP

Ultrasonography

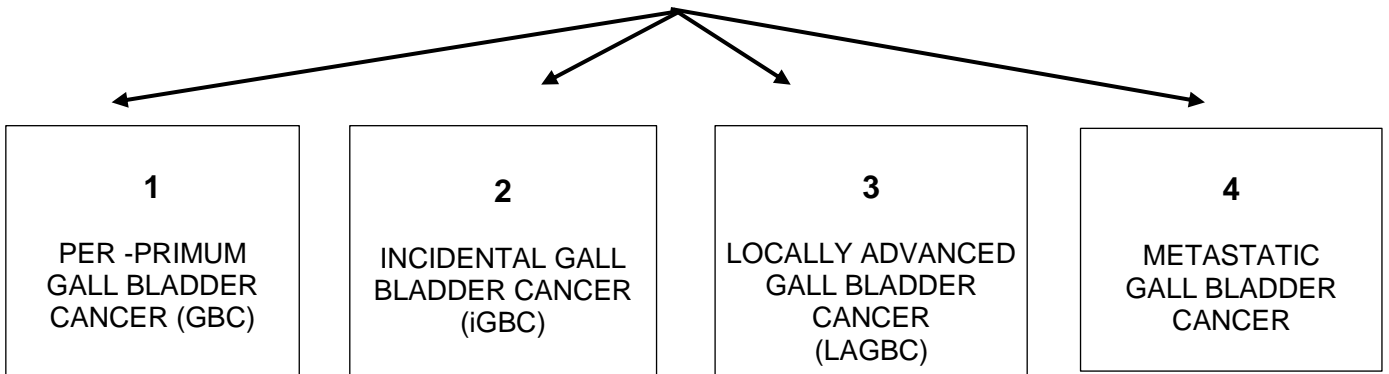
Blood Investigations: Liver function tests, Tumour markers – CA 19-9

CECT Scan of Chest Abdomen and pelvis

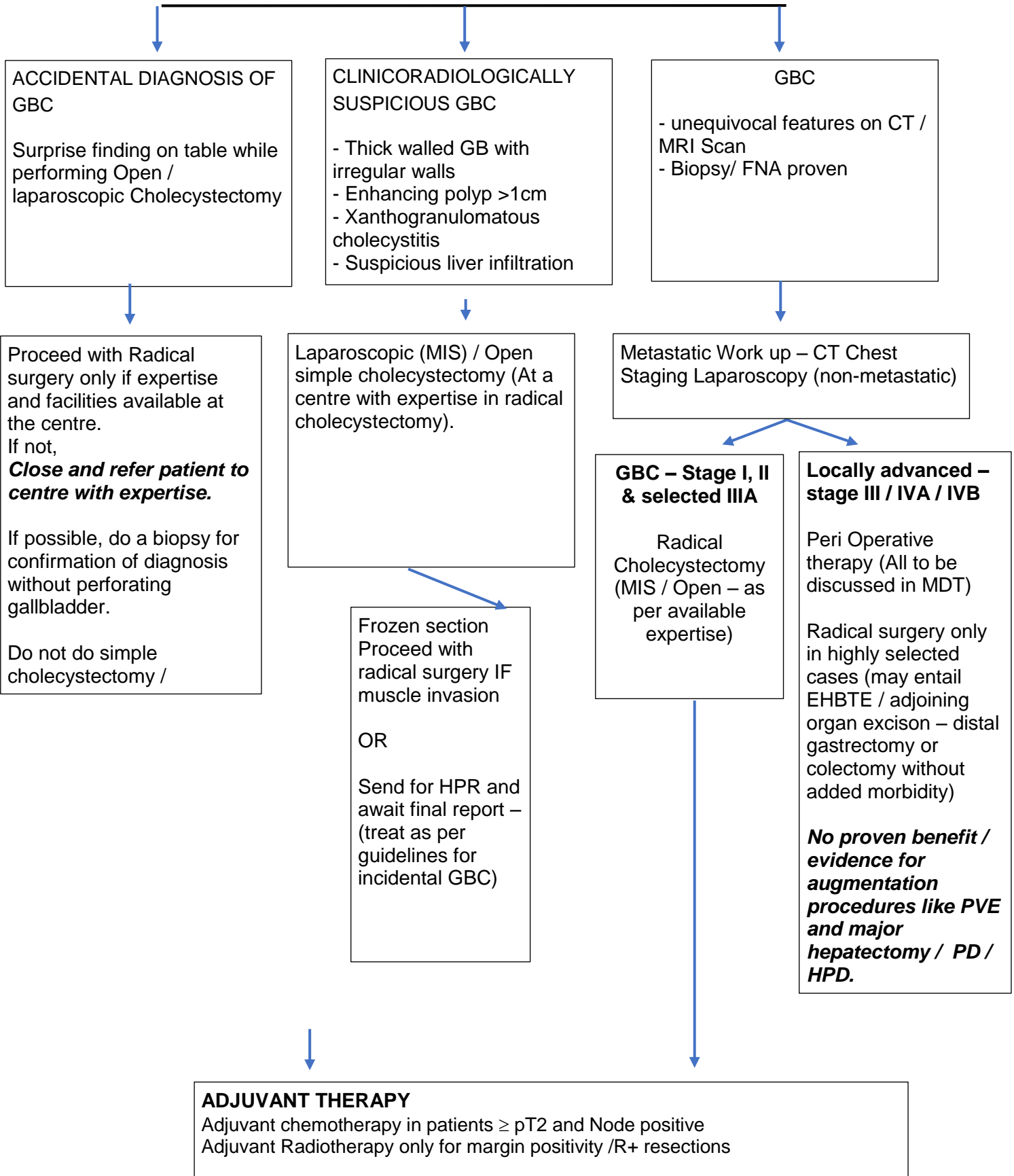
US / CT guided biopsy – if upfront surgery not contemplated/ metastatic disease

Optional: MRI with MRCP in patients presenting with OJ

Whole body PET CECT Scan.



1. PER PRIMUM GBC



RADICAL/EXTENDED CHOLECYSTECTOMY : encompasses removal of Gall bladder along with excision of GB fossa of the Liver – minimum 2.5 cms wedge of liver (extended) or formal segment 4b & 5 (radical) and flush ligation of cystic duct with bile duct (frozen section regulated negative cystic duct margin) along with periportal and retroduodenal nodal clearance – station 8, 12 and 13

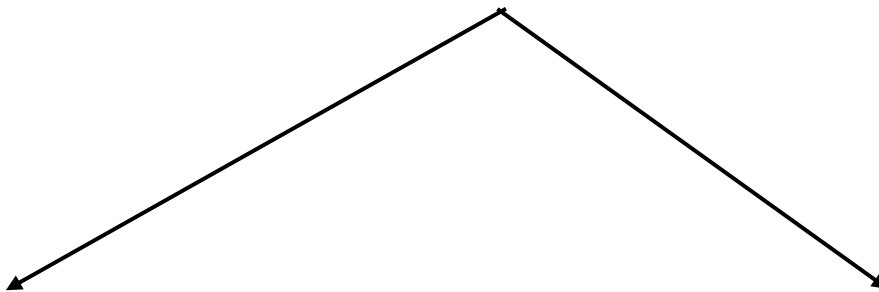
Para aortic lymph nodal sampling (station 16) should be done before proceeding to radical surgery.

2. INCIDENTAL GBC (iGBC)

Diagnosis of Gallbladder cancer based on post operative histopathology of the gallbladder specimen in a case where cholecystectomy (Laparoscopic or open) done for a presumed benign gall bladder pathology



Complete metastatic work up: CT Chest abdomen pelvis / *PET CT if presenting after 6 weeks*
Repeat all labs + Tumour marker CA 19-9
Review of Histopathology – Ideally entire gallbladder to be processed. Note T stage, cystic duct margin and cystic node
Diagnostic laparoscopy if presenting after 4 weeks prior to definitive surgery.



pT1b and above
Stage I, II & selected stage IIIA

Revision Surgery - Revision Radical /
Extended Cholecystectomy

pT3, T4 and N + patients
Stage III, Stage IVA & IVB

Peri-Operative treatment

**To be treated as Locally advanced
GBC.**

**Adjuvant Chemotherapy as per
Stage**

There is no upper and lower time limit for Revision Surgery. Should be done as early as possible and whenever feasible.

No level I or II evidence for Neoadjuvant RT – should be done in trial setting only.

Revision Surgery : Essentially same as Radical cholecystectomy, however, it is important to revise the cystic duct stump to confirm margin negativity on frozen section.

EHBTE can be performed to obtain negative margins or for complete nodal clearance if nodes are densely adherent to bile duct, however routine excision of bile duct is not recommended.

Para aortic lymph nodal sampling is recommended before proceeding to curative surgery

3. LOCALLY ADVANCED GBC (LAGBC)

Identifies high risk group GBC which are likely to relapse or fail at distant sites.

Clinical T 3,4 and any T with node positive disease – stage III and IVA, IVB OR
iGBC with evidence of residual or recurrent disease with no clinic-radiological evidence of distant metastasis

CBC Creatinine, CA 19-9, LFT
Obtaining tissue diagnosis: Biopsy/ FNAB is mandatory to confirm diagnosis
Staging: *Whole body PET CECT Scan*
CECT Scan - Chest, Abdomen and Pelvis

In patients presenting with OJ:
Rule out OJ due to stone disease
MRCP to ascertain the exact level of block

Drainage –
Lower CBD block due to nodal compression – ERCP with plastic/ SEMS placement.
For type I / type II communicating block with roof intact – plastic stent / short SEMS ERC/PTBD
For type II non communicating /III/IV block – Only PTBD , bilateral / unilateral SEMS

Locally advanced unresectable disease unlikely to come up for curative resection

Hilar infiltration with involvement of porta hepatis/ hilar plate with OJ –
Type II non communicating block or III / IV block
Encasement of main PV/LPV/CHA

Locally advanced resectable disease or likely to come up for curative resection

T3, 4 disease, N+
Type I or II communicating block
No Main vessel or contralateral vessel encasement

Staging laparoscopy (optimal)

Chemotherapy with palliative intent.

Can add Radiotherapy as a definitive treatment modality for local control, in absence of metastatic disease

Upfront surgery – Radical cholecystectomy / Revision surgery.
- May entail adjacent/involved organ excision like EHBTE, Distal Gastrectomy or Colectomy

Major resections like hepatectomy, Pancreatoduodenectomy or HPD can be performed in highly selected cases with excellent performance status and good tumor biology

(PREFERRED PATHWAY)

Neoadjuvant chemotherapy – Gemcitabine + Cisplatin (3 – 4 #)
OR
Neoadjuvant Chemo-Radiotherapy (only in trial setting)

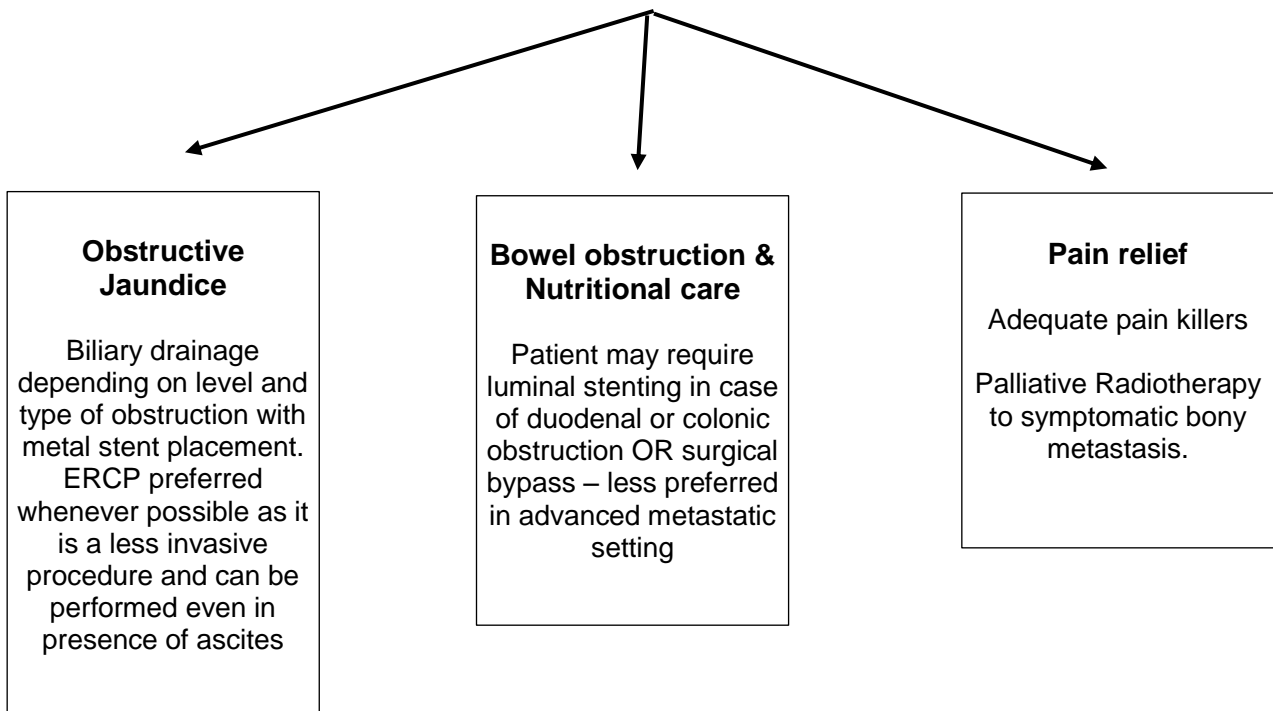
Reassess for possible curative resection

If unresectable or metastatic (PD) – continue palliative chemotherapy
OR
Radical Cholecystectomy / Revision

Adjuvant Chemotherapy

4. METASTATIC GBC

Palliation of:



Palliative chemotherapy – (to add additional IHC, if not confirmed to be an adenocarcinoma on morphology)

1st line chemotherapy: (level I) Gem Cis 3 weekly till progression , response assessment after every 3 to 4 cycles.

(level IIB): Gem cis nab paclitaxel combination

2nd line chemotherapy (level IIB) :

Fluoropyrimidine and or irinotecan / oxaliplatin based chemotherapy

Regorafenib

Bevacizumab erlotinib (Level IIB/III).

References

1. Role of PET CT scan in redefining treatment of incidental gall bladder carcinoma. Goel M, Tamhankar A, Rangarajan V, Patkar S, Ramadwar M, Shrikhande SV. *J Surg Oncol*. 2016
2. Radiological diagnosis alone risks overtreatment of benign disease in suspected gallbladder cancer: A word of caution in an era of radical surgery. Patkar S, Shinde RS, Kurunkar SR, Niyogi D, Shetty NS, Ramadwar M, Goel M. *Indian J Cancer*. 2017
3. Emerging role of multimodality treatment in gall bladder cancer: Outcomes following 510 consecutive resections in a tertiary referral center. Patkar S, Ostwal V, Ramaswamy A, Engineer R, Chopra S, Shetty N, Dusane R, Shrikhande SV, Goel M. *J Surg Oncol*. 2017
4. Aloia TA, Jarufe N, Javle M, et al. Gallbladder cancer: expert consensus statement. *HPB*. 2015.
5. Indian Council of Medical Research consensus document for the management of gall bladder cancer. Shukla HS, Sirohi B, Behari A, Sharma A, Majumdar J, Ganguly M, Tewari M, Kumar S, Saini S, Sahni P, Singh T, Kapoor VK, Sucharita V, Kaur T, Shukla DK, Rath GK. *Indian J Med Paediatr Oncol*. 2015.
6. Agarwal AK, Kalayarsan R, Javed A, et al. The role of staging laparoscopy in primary gall bladder cancer—an analysis of 409 patients: a prospective study to evaluate the role of staging laparoscopy in the management of gallbladder cancer. *Ann Surg*. 2013.
7. Role of routine 16b1 lymph node biopsy in the management of gallbladder cancer: an analysis. Agarwal AK, Kalayarsan R, Javed A, Sakhuja P. *HPB (Oxford)*. 2014 Mar.
8. Al-Temimi MH, Mousa IF, O'connor V, et al. Anatomical hepatic resection versus wedge resection for gallbladder cancer: analysis of multi-center database. *HPB* 2018;20:S20.
9. Achieving margin negative resection—doing less is justified: oncological outcomes of wedge excision of liver in gallbladder cancer (GBC) surgery Shradha Patkar, Vijayraj Patil, M. Rajgopal Acharya, Sagar Kurunkar, Mahesh Goel *Chin Clin Oncol* 2019
10. Biliary obstruction in gall bladder cancer is not sine qua non of inoperability. Agarwal AK, Mandal S, Singh S, Bhojwani R, Sakhuja P, Uppal R. *Ann Surg Oncol*. 2007 Oct.
11. Capecitabine compared with observation in resected biliary tract cancer (BILCAP): a randomised, controlled, multicentre, phase 3 study. Primrose JN, Fox RP, Palmer DH, Malik HZ, Prasad R, Mirza D, Anthony A, Corrie P, Falk S, Finch-Jones M, Wasan H, Ross P, Wall L, Wadsley J, Evans JTR, Stocken D, Prasad R, Ma YT, Davidson B, Neoptolemos JP, Iveson T, Raftery J, Zhu S, Cunningham D, Garden OJ, Stubbs C, Valle JW, Bridgewater J; BILCAP study group. *Lancet Oncol*. 2019 May;20(5):663-673.
12. Gemcitabine-cisplatin (GC) as adjuvant chemotherapy in resected stage II and stage III gallbladder cancers (GBC): a potential way forward. Ostwal V, Swami R, Patkar S, Majumdar S, Goel M, Mehta S, Engineer R, Mandavkar S, Kumar S, Ramaswamy A. *Med Oncol*. 2018
13. Role of Adjuvant Chemotherapy in Resected T2N0 Gall Bladder Cancer. Kattepur AK, Patkar S, Goel M, Ramaswamy A, Ostwal V. *J Gastrointest Surg*. 2019.

14. Neoadjuvant chemotherapy in patients with locally advanced gallbladder cancer Sirohi B, Mitra A, Jagannath P, Singh A, Ramadwar M, Kulkarni S, Goel M, Shrikhande SV. *Future Oncol.* 2015
15. Selvakumar VP, Zaidi S, Pande P, et al. Resection after neoadjuvant chemotherapy in advanced carcinoma of the gallbladder: a retrospective study. *Indian J Surg Oncol* 2015.
16. Neoadjuvant Chemoradiation Followed by Surgery for Locally Advanced Gallbladder Cancers: A New Paradigm. Engineer R, Goel M, Chopra S, Patil P, Purandare N, Rangarajan V, Ph R, Bal M, Shrikhande S, Shrivastava SK, Mehta S *Ann Surg Oncol.* 2016
17. A phase III randomised clinical trial of perioperative therapy (neoadjuvant chemotherapy versus chemoradiotherapy) in locally advanced gallbladder cancers (POLCAGB): study protocol. Engineer R, Patkar S, Lewis SC, Sharma AD, Shetty N, Ostwal V, Ramaswamy A, Chopra S, Agrawal A, Patil P, Mehta S, Goel M. *BMJ Open.* 2019
18. Outcome of neoadjuvant chemotherapy in "locally advanced/borderline resectable" gallbladder cancer: the need to define indications. Chaudhari VA, Ostwal V, Patkar S, Sahu A, Toshniwal A, Ramaswamy A, Shetty NS, Shrikhande SV, Goel M. *HPB (Oxford).* 2018
19. Treatment of advanced Gall bladder cancer in the real world-can continuation chemotherapy improve outcomes? Ostwal V, Pinninti R, Ramaswamy A, Shetty N, Goel M, Patkar S, Mirani J, Nashikkar C, Banavali S. *J Gastrointest Oncol.* 2017
20. Valle J, Wasan H, Palmer DH, Cunningham D, Anthony A, Maraveyas A et al. (2010) Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *N Engl J Med* 362:1273–1281.
21. SWOG S0809: A Phase II Intergroup Trial of Adjuvant Capecitabine and Gemcitabine Followed by Radiotherapy and Concurrent Capecitabine in Extrahepatic Cholangiocarcinoma and Gallbladder Carcinoma. Ben-Josef E, Guthrie KA, El-Khoueiry AB, Corless CL, Zalupski MM, Lowy AM, Thomas CR Jr, Alberts SR, Dawson LA, Micetich KC, Thomas MB, Siegel AB, Blanke CD. *J Clin Oncol.* 2015 Aug 20;33(24):2617-22. doi: 10.1200/JCO.2014.60.2219. Epub 2015 May 11. PMID: 25964250
22. Second-Line Palliative Chemotherapy in Advanced Gall Bladder Cancer, CAP-IRI: Safe and Effective Option. Ramaswamy A, Ostwal V, Pande N, Sahu A, Jandyal S, Ramadwar M, Shetty N, Patkar S, Goel M, Gupta S. *J Gastrointest Cancer.* 2016