Meta-analysis in Gastric Carcinomas

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Epidemiology.

- The **incidence** of gastric cancer **highest** in **North Eastern states**, such as Mizoram and Sikkim.
- Among the **five most common cancers** affecting young Indian men and women (age, 15–44 years).
- **Second** most common cause of **cancer-related deaths** among Indian men and women.
- A **multidisciplinary approach** : cornerstone in achieving the best outcome for patients with resectable gastric cancer.

Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, *et al. Cancer Incidence in Five Continents. Vol. 9. IARC Scientific* Publications. 2007. p. 160.
Khuroo MS, Zargar SA, Mahajan R, Banday MA. High incidence of oesophageal and gastric cancer in Kashmir in a population with special personal and dietary habits. Gut 1992;33:11-5.
Kalyani R, Das S, Kumar ML. Pattern of cancer in adolescent and young adults: A ten year study in India. Asian Pac J Cancer Prev 2010;11:655-9.

Current Recommendations

T1N0 and selective T2N0	SURGERY ALONE
T2-T4/ N+,RESECTABLE	SURGERY FOLLOWED BY CTRT PRE OP CT SX POST OP CT
UNRESECTABLE	CTRT CHEMOTHERAPY ALONE BEST SUPPORTIVE CARE
	CHEMOTHERAPY ALONE BEST SUPPORTIVE CARE PALLIATIVE RT

Uncertainties /Controversies

???????

Meta-analysis is a **quantitative** approach for **systematically** combining results of **previous research** to **arrive at conclusions** about the body of research.

Contents :

Meta-anlysis related to

1) *H. pylori* eradication .
2) EUS & staging.
3) Laparoscopic Gastrectomy vs Open Gastrectomy.
4) D1 vs D2
5) Perioperative vs adjuvant chemotherapy.
6) Adjuvant chemo radiotherapy vs chemotherapy.
7) Adjuvant chemotherapy.
8) Sx alone vs with adjuvant chemotherapy.
9) Surgery with vs. without intraperitoneal chemotherapy(IPC)
10) Efficacy and safety of Taxanes Based CT
11) Role of Palliative RT
12) Gastrectomy in Stage IV .
13) BSC vs Chemotherapy.

Eradication of *H Pylori* and Gastric cancer?

- Helicobacter pylori (*H. pylori*) is associated with an increased risk of gastric adenocarcinoma and gastric mucosa associated lymphoid tissue (MALT) lymphoma and a decreased risk of esophageal adenocarcinoma.

Eradication of Helicobacter pylori and Gastric Cancer:A Systematic Review and Meta-analysis of Cohort Studies. Eva Doorakkers, Jesper Lagergren et alJNCI J Natl Cancer Inst (2016) 108(9): djw132

Results:

- **Eight** cohort studies : **31,553 patients**.
- Indicates that **eradication** therapy for H. pylori **prevents gastric cancer.**
- H. pylori eradication in relation to the risk of gastric MALT lymphoma and esophageal cancer is currently too limited to enable meta-analyses.

Eradication of Helicobacter pylori and Gastric Cancer:A Systematic Review and Meta-analysis of Cohort Studies. Eva Doorakkers, Jesper Lagergren et alJNCI J Natl Cancer Inst (2016) 108(9): djw132

Studies comparing eradication therapy to no treatment & comparing successful to unsuccessful treatment.

Eradiated vs not eradicated

Successful vs not successful

Eradication of Helicobacter pylori and Gastric Cancer:A Systematic Review and Meta-analysis of Cohort Studies. Eva Doorakkers, Jesper Lagergren et alJNCI J Natl Cancer Inst (2016) 108(9): djw132

Meta-analysis : utility of EUS for preoperative staging for gastric cancer

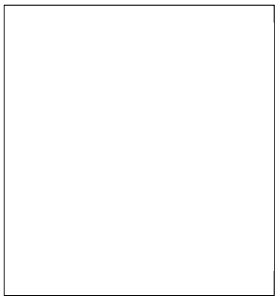
- Twenty-two articles
- EUS pooled **accuracy for T staging** was **75%** with a moderate Kappa (0.52).
- EUS was most accurate for **T3** disease, followed by **T4**, T1, and T2.
- EUS pooled **accuracy** for **N staging** was **64%**, sensitivity was 74%, and specificity was 80%.
- Significant **heterogeneity** between the included studies.

Conclusion: EUS is a moderately accurate technique that seems to describe advanced T stage (T3 and T4) better than N or less advanced T stage.

A systematic review and meta-analysis of the utility of EUS for preoperative staging for gastric cancer Roberta Cardoso Natalie Coburn et al Gastric Cancer (2012) 15 (Suppl 1):S19–S26

EUS T4 Staging

EUS N staging



A systematic review and meta-analysis of the utility of EUS for preoperative staging for gastric cancer Roberta Cardoso Natalie Coburn et al Gastric Cancer (2012) 15 (Suppl 1):S19–S26

Laparoscopic Gastrectomy(LG) vs. Open Gastrectomy(OG)

Management of advanced gastric cancer: An overview of major findings from meta –analysis Xiaolong Qi et al Oncotarget, Vol. 7, No. 47

Laparoscopic Gastrectomy (LG) vs Open Gastrectomy (OG)

- At least ***9*** meta-analyses *and* a Cochrane review compared the outcomes of LG versus OG.
- Number of harvested lymph nodes, OS and DFS were similar .
- Six analyses studied recurrence data and found it to be similar.
- LG had lower intraoperative blood loss, reduced risk of postoperative complications and shorter hospital stay.
- The Cochrane review also had similar findings, though the authors noted wide CIs for the parameters studied. They suggested more data be accrued before drawing a definite conclusion.

Takeaway: LG may considered a safe alternative to OG for AGC with a lower complication rate and enhanced postoperative recovery.

Management of advanced gastric cancer: An overview of major findings from meta –analysis Xiaolong Qi et al Oncotarget, Vol. 7, No. 47

Type of Surgery: D1 vs D2 dissection

- Several RCT's + least **3 meta-analyses** have addressed this question.
- Individual studies have had conflicting results, with some suggesting no difference in outcomes and others vice versa.
- Meta-analyses have found a **definite trend towards improved survival** and gastric cancer related mortality with a D2 dissection.
  - In general, east Asian studies have shown improved outcomes while Western literature is more critical of the approach.

Present consensus: **D2 dissection should be done** wherever the experience and post-operative care is available to manage the greater morbidity associated with it (ESMO, NCCN).

Management of advanced gastric cancer: An overview of major findings from meta –analysis Xiaolong Qi et al Oncotarget, Vol. 7, No. 47

NEOADJUVANT/PERIOPERATIVE vs ADJUVANT ??

3 MAJOR TRIALS

MAGIC

French FNLCC/FFCD

EORTC 40954

MAGIC TRIAL

ELIGIBILITY CRITERIA

- ANY AGE
- T2 OR HIGHER
- PS: 0 OR 1
- ADENOCARCINOMA OF STOMACH OR DISTAL ESOPHAGUS
- NO EVIDENCE OF DISTANT METASTASIS

MAGIC TRIAL

JULY 1994 TO APRIL 2002

TOTAL 503 PATIENTS

250 patients	253 patients
Perioperative chemotherapy & Sx	**Surgery only**

- **Epirubicine**
- **Cisplatin**
- **Infusional 5FU**

PFS OS

5 yr survival 36% Vs 23%

SUMMARY

- OS and PFS: Significantly better with perioperative chemotherapy.
- Estimated improvement in 5-year survival: 13% (23% → 36%).
- Local failure and distant metastases were both lower 14% Vs 21% & 24% Vs 37% respectively.

The UK NCRI MAGIC Trial of Perioperative Chemotherapy in Resectable Gastric Cancer: Implications for Clinical Practice Yu Jo Chua, Annals of Surgical Oncology 14(10):2687–2690

Limitations of Magic Trial .

- Non standardized surgery
- Inaccurate preoperative staging
- Higher proportion of patients in chemotherapy arm undergo potentially curative surgery (79% VS 70%).
- More patients in the chemotherapy arm had lower stage disease: T1/2 (52 vs 37%) and N0/1 (84 vs 71%).
- Only 104 (42%) patients were able to complete protocol treatment.

The UK NCRI MAGIC Trial of Perioperative Chemotherapy in Resectable Gastric Cancer: Implications for Clinical Practice Yu Jo Chua, Annals of Surgical Oncology 14(10):2687–2690

FRENCH FNCLCC TRIAL

November, 1995 - December, 2003

All patients underwent **D2 resection** which is the standard surgical procedure in gastric carcinoma.

CHEMOTHERAPY USED WAS CISPLATIN AND 5FU

5YR DFS
34% VS 19%

5YR OS
38% VS 24%

AFTER MEDIAN FOLLOW UP OF 5.7 YEARS

- Significant improvement in DFS and OS with perioperative chemotherapy.
- Most common toxicity: Neutropenia and nausea/vomiting.

Neoadjuvant chemotherapy (NACT) vs. Upfront Surgery

- **Two meta-analyses** compared the outcomes of surgery in combination with NACT versus no therapy before surgery.
- Both of them **favored NACT** in terms of **OS.**
- One of them also **favored NACT** in terms of **3-year PFS.**
- Both meta-analyses demonstrated that the **resection rate** was **higher** for **NACT group** than for control group while the perioperative mortality was similar.
- One of them also noted that **NACT** had a significant **down-staging effect** on AGC.
- NACT could improve the tumor resection rate and the survival rate in AGC patients **without increasing** the **operative risk**.

Meta-analysis regarding NACT

- NACT associated with significant OS & PFS improvement.
- NACT : ↑↑ R0 Resection rate.
- No worsening of operative complications, perioperative mortality, or grade 3 or 4 adverse effects.

Management of advanced gastric cancer: An overview of major findings from meta –analysis Xiaolong Qi et al Oncotarget, Vol. 7, No. 47

Zhao et al. BMC Cancer (2016) 16:631

- 11 studies : Five RCT + six clinical controlled trials (**1,240pts**).
- First metaanalysis that compares PC with AC in GC.
- PC vs AC had significantly **better prognosis** (HR, 0.74; 95 % CI, 0.61 to 0.89; **P < 0.01**).
- NAC: better in

Comb chemotherapy : (HR, 0.59; 95 % CI, 0.46 to 0.76; **P < 0.01**) vs

5FU monotherapy : (HR, 0.93; 95 % CI, 0.56 to 1.55; **P = 0.84**)

- PC group :trend towards a ↑radical resection rate (RR, 1.10; 95 % CI, 0.96 to 1.27; P = 0.17)
- **No** significant differences in the **post-operative complication** rates (relative risk,0.98;95%CI,0.63to1.51; **P = 0.91**)
- **Adverse effects** : **not** significantly **different** between the two study groups (P > 0.05 for all the comparisons.)

RCT vs CCT

China vs Japan

NAC Regimen

Monotherapy

Combination CT

NAC significant better in the studies that used
Combination chemotherapy : (HR, 0.59; 95 % CI, 0.46 to 0.76; P < 0.01) vs
Fluoropyrimidine monotherapy : (HR, 0.93; 95 % CI, 0.56 to 1.55; P = 0.84)

Meta-analysis of Hazard ratio for radical resection rate.

Meta-analysis of postoperative complication rate

Adjuvant Chemoradiation

3 RANDOMIZED TRIALS

INT 0116/ SWOG 9008 Macdonald regimen

CALGB 80101

ARTIST

Macdonald regimen

T3 or higher
And/node +ve
R0 resection

RADIOCHEMOTHERAPY CONSISTED OF BOLUS FLUOROURACIL AND LEUCOVORIN BEFORE, DURING, AND AFTER RADIOTHERAPY.

STUDY DESIGN

DAY 1 TO 5
LEUCOVORIN(20mg) AND 5 FLUOROURACIL(425mg)

DAY 28

FU 400 mg/m²/d and LV 20 mg/m²/d was given the first four and the last three days of radiotherapy.

1 MONTH AFTER RT

5 Yr O S
43% Vs 28%
IN FAVOUR OF CTRT

3 Yr DFS
48% VS 31%
IN FAVOUR OF CTRT

DISTANT RELAPSE WAS 16% VS 18%
REGIONAL RELAPSE WAS 22% VS 39%

Even after 10 years of follow up the survival advantage WITH CTRT is better than surgery alone.

- **3yr OS was 50% vs 41%**
- **3yr RFS was 48% vs 31%**
- **Toxicity was more with CTRT.**

Conclusion:

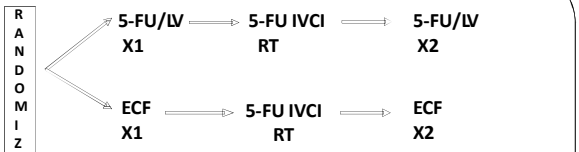
- **CTRT significantly decreases the locoregional Failure.**

Limitations:

- **D2 dissection was only performed in 10% of cases.**
- **Only 64% of cases completed the treatment and 17% discontinued treatment due to toxicity.**

CHEMORADIOTHERAPY PLUS SURGERY FOR GASTRIC ADENOCARCINOMA J JOHN S. MACDONALD, M.D., STEPHEN R. S MALLEY, M.D. N Engl J Med, Vol. 345, No. 10 September 6, 2001

Postop adjuvant chemoradiation for gastric or GE junction Adeno Ca **Intergroup CALGB 80101**

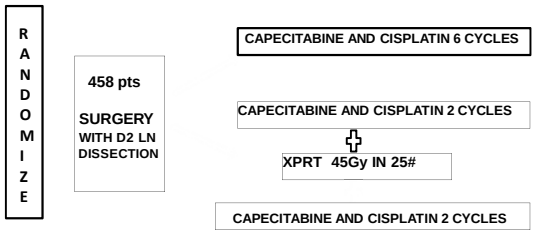


5-FU/LV: 5-FU 425 mg/m d1-5, LV 20 mg/m d1-5
RT: 45 Gy (1.8 Gy X 25 fractions) with 5-FU 200 mg/m /d CI
ECF (pre-RT): Epirubicin 50 mg/md1, Cisplatin 60 mg/md1, &C5-FU 200 mg/m /d1-21
ECF (post-RT): Epirubicin 40 mg/mCisplatin 50 mg/m5-FU 200 mg/m /d CI d1-21

NO DIFFRENCE IN OS
P=0.80

NO DIFFERENCE IN DFS
P=0.99

ARTIST



NO DIFFERENCE IN DFS & OS

- Subset analysis indicate a significantly **better DFS** with chemoradiotherapy in those with **node-positive** disease (three-year DFS 76 versus 72 %, **p = 0.004**).

META- ANALYSIS Major Randomized Trial of Chemo radiotherapy

Trial	Years	Patients: N,Stage,Location	Randomization	Primary Outcome	Comments
INT-0116	1991-1998	556;Stage Ib+;stomach/GEJ	1.Surgery 2.Surgery→CRT	Median OS 35 months 27 months	1. 85% pN+ 2. Majority Do/D1 Ln dissection 3. Outdated RT technique
MAGIC	2002-2006	503;Stage II/III;Stomach/GEJ	1.ECF→Surgery 2.ECF→Surgery ECF	5-year OS 23% 36%	1. Only 3 cycles of ECF 2. Poor treatment compliance(42%)
POET	2001-2011	126;Stage T3N+M0;Cardia/GEJ	1.PLF.Surgery 2.PLF→CRT→Surgery	3-year OS 28% 47% (NSS)	1.Underpowered(closed early) 2.CRT:30 Gy,concurrent EP
ARTIST	2004-2008	458;Stage Ib+;Stomach/GEJ	1.Surgery (D2)→XP 2.Surgery (D2)→XP/CRT/XP	3-year DFS 74.2% 78.2% (NSS)	1.OS not analysed 2.SS DFS benefit in pN-positive patients
CRITICS	2007-2015	788;Stage Ib+;Stomach/GEJ	1.ECC→Surgery→ECC 2.ECC→Surgery→CRT	5-year OS 41.3% 40.9%	1.Abstract only 2.Poor treatment compliance(CT:47%;CRT:52%)
TOPGEAR	2009-2017	752 (est);Stage Ib+;Stomach/GEJ	1.ECF→Surgery→ECF 2.ECF→CRT→Surgery ECF	5-year OS	1.Pending presentation/publication 2.Accrual expected December 2017
ARTIST 2	2013-2019	900 (est);pN Positive;Stomach/GEJ	1.Surgery (D2)→S-1 2.Surgery (D2)→SOX 3.Surgery (D2)→SOX/CRT/SOX	3-year DFS	1.Pending presentation/publication 2.Accrual expected 2019

Significantly improved 5-yr DFS and Local control with CTRT.
Trend towards improved overall survival but that is not statistically significant

Adjuvant Chemotherapy

2 TRIALS

JAPANESE S-1 trial

CLASSIC trial

JAPANESE S-1 TRIAL

Stage II , III
Potentially resectable
Sx with D2 lymphadenectomy

S1: 3 drug combination with principal agent **tegafur**.

OS

Primary end point: **OS**
Median FU: **5 years**

RFS

Results	Surgery + adjuvant S-1	Surgery alone
OS	71.7%	61.1%
RFS	65.4%	53.1%

Conclusion: Adjuvant S1 improves survival for Stage II/III gastric cancer.

CLASSIC TRIAL

RANDOMIZE

1035 pts

SURGERY WITH D2 LN DISSECTION

AT LEAST 15 LN EXTRACTED

CAPECITABINE AND OXALIPLATIN 8 CYCLES

520 PATIENTS — Capcitabine 1000mg/m D1-14, Oxaliplatin 130 mg/m

NO ADJUVANT THERAPY

515 PATIENTS

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3 YEAR DFS 74% VS 59%

P < 0.0001

3 YEAR OS : 83% VS 78%
5 YEAR OS : 78% VS 69%

P = 0.0493

9 TIMES MORE GRADE 3 & 4 TOXICITIES IN CT ARM.
ONLY 67% OF PATIENTS RECEIVED ALL 8 CYCLES OF CT.
90% OF PATIENTS REQUIRE CT DOSE MODIFICATION.

Meta-analysis : Adjuvant Chemotherapy

First Author	Journal (year)	Comparisons	OS	SR,DFS,RFS,PFS,Recurrence, TTF,TTP	Other	Major Comments
Sun J(36)	BMC Cancer(2013)	(Include palliative gastrectomy with vs. without AC).	**Favour palliative gastrectomy with AC.**	N A.	N A.	Palliative gastrectomy combined with chemotherapy maight improve survival.
Sun P(57)	BR J Surg (2009)	Surgery with vs. without AC	**Favour surgery with AC.**	N A	N A	Postoperative chemotherapy could improve OS after radical surgery for gastric cancer.

Surgery with vs. without intraperitoneal chemotherapy (IPC)

- **Two meta-analyses** compared the outcomes of surgery combined with IPC versus surgery without IPC.
- One of the meta-analyses revealed IPC significantly **improve 1-, 2-, 3-year OS** but not 5-year OS.
- Another meta-analysis on adjuvant IPC demonstrated that hyperthermic intraoperative intraperitoneal chemotherapy (HIIPC) with or without early postop intraperitoneal chemotherapy (EPIPC) after gastrectomy was associated with **improved OS**; Best therapy in Positive peritoneal metastasis.

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Meta-analysis: Surgery with or without IPC

First Author	Journal	Comparisons	OS	SR,DFS,RFS,PFS,Recurrence,TTF,TTP	Other	Major Comments
Coccolini F(16)	Eur J Surg Oncol 2014	Surgery with vs. without IPC	**1,2,3, year: favour surgery+ IPC;** **5-year:** statistically similar	Overall recurrence, peritoneal recurrence, haematogenous metastasis: favour surgery+ IPC Lymph nodal recurrence: statistically similar	Mortality:1-,2-,3-year: Favour surgery+IPC; 5year: Statistically similar 2-,3-year in patients with loco-regional nodal matastasis,1,2-year in patients with serosal infiltration:favour surgery+IPC,Morbidity:higher in surgery alone.	IPC had positive effect on peritoneal recurrence and distant metastasis. Morbidity rate is incremented by IPC. Loco-regional lymph-nodes invasion in patients affected by AGC was not a contraindication to IPC.
Yan TD(58)	Ann Surg Oncol 2007	Surgery with vs. without IPC	Favour surgery with HIIPC or with HIIPC+ EPIPC (but statistically similar between surgery with NIIPC,EPIPC or DPIPC and surgery without IPC)	Peritoneal recurrence)surgery with HIIPC or NIIPC vs. control): statistically similar.	Perioperative mortality: statistically similar. Risk of intra-abdominal abscess, neutropenia: higher in IPC+ surgery.	HIIPC with or without EPIPC after resection of AGC improved the overall survival.However,increased risk of intra-abdominal abscess and neutropenia were also demonstrated.

- Intraoperative intraperitoneal chemotherapy (**IIPC**) with **adjuvant chemotherapy** showed a trend toward i***mprovement In overall survival*** (HR 0.70; 95 % CI 0.47–1.04; p = 0.08).
- A recent randomized controlled trial examining extensive intraperitoneal lavage (EIPL) with IIPC showed a significant improvement in overall survival (**5-year overall survival, 43.8** % for EIPL-IPC group compared with **4.6 %for IPC group**).
- Given its superiority in the quantity of RCT studies, the results of the **meta-analysis by Coccolini** might be more reliable.
- Locoregional Lymph node invasion was not a contraindication
- **Conculsion: IPC** had **positive effect** on **overall and peritoneal recurrence** and **distant metastasis**.

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Advanced Gastric Cancer

Unresectable, recurrent and/or metastatic disease

Chemotherapy
Advanced Gastric Cancer: Taxane based CT

- In the palliative setting, 5FU based regimens are mostly employed, but taxanes are now increasingly being used by several researchers.
- Shi et al analyzed data from 11 studies (6 randomized, 5 non-randomized) and evaluated data from 1932 patients and compared:
  1. Non taxane regimen vs same regimen + Taxane
  2. Taxane vs non taxane chemotherapy
- 1st comparison: OS, PFS and Overall response rate (ORR) were all better with taxane.
- 2nd comparison: PFS and ORR was better but not the OS. Toxicity was higher with taxanes, but not significantly so.

Conclusion: Adding taxanes to current first-line treatment options for AGC can improve OS, PFS, and ORR; however, these increase the risk of toxicity and options should be discussed with the patient.

Chemotherapy
Advanced Gastric Cancer: Cisplatin or not?

- 5-FU based chemotherapy is the main treatment for advanced gastric cancer and has been demonstrated to improve OS in a Cochrane analysis.
  - Studies have shown that adding other agents (other than cisplatin) also improves outcomes, most notably oxaliplatin.
- Petrelli et al compared Cisplatin based regimens to chemotherapy in which Cisplatin was replaced by a different drug.
  - 14 studies (5 randomized, 9 phase II), 2981 patients
  - They found non-cisplatin regimens to have significantly better outcomes:
    - OS: HR 0.79, 95% CI 0.68 – 0.92
    - PFS: HR 0.77, 95% CI 0.66 - 0.90

Conclusion: Combination chemotherapy in which cisplatin is replaced by new drugs improve outcomes and should therefore be strongly considered in the metastatic setting.

Role of Palliative RT

- A meta-analysis of **7 studies of palliative RT**
- Various dose-fractionation schedules.
- Bleeding: No difference in response rate (BED) of ≥ 39Gy vs low BED < 39Gy.
- Upto 15% patients had Grade 3+ toxicities.

	ORR
Bleeding	74%
Pain	67%
Obstructive symptoms	68%

Conclusion: More than two-thirds of patients receiving RT in the palliative setting would have a benefit, and low BED regimens appear to be adequate for symptom palliation.

Palliative radiotherapy for gastric cancer: a systematic review and meta-analysis Jeremy Tey1, Yu Yang Soon et al Oncotarget, 2017, Vol. 8, (No. 15), pp: 25797-25805.

Gastrectomy for Stage IV Gastric Cancer A Systematic Review and Meta-analysis

- 50% patients with non-resected advanced gastric carcinoma develop severe tumor-related complications that may merit surgical resection.
- Lasithiotakis et al :**19 studies (2911 patients)** who underwent local surgery as a part of treatment for metastatic disease.
- Patients who underwent resection had a better 1 year OS vs conservative management (OR 4.9, 95% CI 3.2-7.5), and also when compared to non resectional treatment (OR 2.6, 95% CI 1.7 – 4.3).
- However, this is all from non-randomized data.

Conclusion: Benefit cannot be ruled out, but no randomized evidence at present; not routinely recommended.

Gastrectomy for Stage IV Gastric Cancer.A Systematic Review and Meta-analysis KONSTANTINOS LASITHIOTAKIANTICANCER RESEARCH 34: 2079-2086 (2014)S

Chemotherapy vs. basic supportive care (BSC)

- In patients with relapsed/poorly responding disease, several studies have shown that there is an OS benefit with second line chemotherapy.
  - A meta-analysis of 3 such studies (janowitz et al, *BJC* 2016) was doe on patients who had failed after 1st line chemotherapy with CDDP/5FU based regimens.
  - 2nd line chemotherapy significantly improved OS (HR for death 0.63) and older patients with a better PS and non-metastatic disease have a better outcome.
  - QoL data was reported in only one of the studies.
- For third line chemotherapy, Chan et al published a review of 6 studies involving 890 patients.
  - They reported a significant, though small OS benefit (3.2m → 4.8m). PFS, ORR and disease control rate were also better. QoL data was, however, not reported.
- Second and 3rd line chemotherapy does provide benefit, but an analysis is required to assess the cost and morbidity associated with it.

Conclusion: Can consider 2nd/3rd line chemotherapy; especially for patients with a good PS. Patient should be involved in the decision making process.

CONCLUSION

- Multimodality treatment (MMT) should be the norm for management of gastric cancer.
- For locally advanced disease, gastrectomy remains the mainstay of treatment. Laparoscopic gastrectomy with D2 nodal dissection should be considered standard of care.
- Adjuvant treatment improves outcomes (for advanced disease).
  - D1 or D0 nodal dissection: Chemoradiotherapy (CRT)
  - D2 dissection: CRT if node positive, chemotherapy alone if node negative.
- Neoadjuvant/perioperative chemotherapy should be considered for resectable disease. For unresectable disease, Neoadjuvant CRT will often provide the opportunity for a curative resection.
- All 3 treatment modalities have a role in palliation; chemotherapy and radiotherapy more so than surgery.

THANK YOU