



# Current management and controversies in management of T4 cancers of the colon – a narrative review of the literature

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**Abstract:** Colorectal cancer is the third most common malignancy and represents the third most likely cause of cancer related deaths worldwide with approximately 10% of patients with locally advanced colon cancer (LACC) presenting with peritoneal involvement (T4a) or invasion of adjacent organs (T4b) at the time of diagnosis. Accurate pre-operative staging is paramount, and while CT and MRI scans are useful in identifying lymph nodal involvement and distant metastasis, there is an inherent inability to accurately differentiate true invasion from the simple, inflammatory adherence to the neighbouring structures with these existing imaging modalities. Despite the advanced nature of this disease, extended and multivisceral resections with clear margins (R0 resection) combined with appropriate adjuvant treatments have been shown to result in good oncological outcomes and offer patients a real chance of cure. There is emerging evidence in the use of neoadjuvant chemotherapy (NAC) and/or radiotherapy in T4a/T4b colon cancers, these therapies have been successfully utilised in patients with non-obstructing LACC and appear to be a safe and effective way to increase chances of achieving a R0 resection without significant morbidity or mortality. This review is focused on preoperative workup, conventional treatment strategies and controversies in advanced T4 colon cancers.

**Keywords:** T4 colon cancer; neoadjuvant chemotherapy (NAC); neoadjuvant radiotherapy (NRT); extended colonic resections; multivisceral resections; pre-operative staging

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## Introduction

Colorectal cancer is the third most common malignancy in the world, with approximately 10% of patients with locally advanced disease with peritoneal involvement (T4a) or invasion of adjacent organs (T4b) at the time

of diagnosis (1,2) and accounts for third leading cause of cancer related deaths in both genders (3). The prognosis of patients with colon cancer largely correlates to their TNM staging with a 5-year disease specific survival of all T4 tumours being 75% (4), however, there is significant

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variance within this group with T4a tumours having a significantly higher 5-year survival than T4b tumours (61% *vs.* 46%) (5,6) underscoring the importance of accurate pre-operative staging. Important questions remain regarding the utilisation of neoadjuvant chemotherapy (NAC) and/or neoadjuvant radiotherapy (NRT) to increase their chances of achieving a R0 resection.

We present the following article in accordance with the Narrative Review reporting checklist (available at <http://dx.doi.org/10.21037/dmr-20-74>).

## Methods

A literature search was performed for all English articles in this field utilising the MEDLINE (via PubMed) and EMBASE (via OvidSP) databases. Ongoing trials were identified via the clinical trials registry: <https://clinicaltrials.gov>. All natures of studies; prospective randomised controlled trials, non-randomised prospective trials, retrospective studies, case reports, reviews, meta-analyses and conference abstracts were included. Additional manual searches of relevant articles were also conducted. Key words used included “neoadjuvant chemotherapy”, “neoadjuvant chemoradiotherapy”, “neoadjuvant radiotherapy” in “locally advanced colon cancer”, “high risk T3” and “T4 colon cancer”. Studies referring to locally advanced colon cancer (LACC) with metastases were excluded.

## Pre-operative work up

European Society of Medical Oncology (ESMO) and National Comprehensive Cancer Network (NCCN) guidelines for preoperative work up include baseline blood tests including carcino-embryonic antigen (CEA), colonoscopy preoperatively if possible, however in an emergent setting this can be performed post operatively, and computed tomography (CT) scan of the chest, abdomen, and pelvis (7). In the case of equivocal CT findings or contraindications to IV contrast, the NCCN recommend positron emission tomography (PET) scan to provide further clarification (8).

Clinically, since T4 tumours are locally advanced, many of them will be diagnosed in an emergent setting with incidence being up to 69% compared with 26% in the elective group (9). In the case of intestinal obstruction or peritonitis due to tumour perforation, preoperative CT scans will adequately describe the lesion responsible but may not accurately discern the full extent of the tumour's

local invasion or the presence of nodal involvement.

In elective cases, a recent meta-analysis by Nerad *et al.* (10) found that CT overstaged one-third of all patients with an overall sensitivity of 90% in detecting tumour invasion beyond the bowel wall but a specificity of 69%. To date, no studies are able to offer an explanation for the low specificity, however, it is suggested that radiologists, to minimize the risk for under-staging, interpret minimal pericolonic fat stranding due to benign desmoplastic reaction as tumour invasion. This is a widely recognised problem in colorectal staging (11).

Abdominal CT is, however, is very important in detecting distant metastases, especially in T4 colon cancers as the risk of distant metastases is high (up to 45% of the cases), as well as the risk of nodal involvement (up to 65% of the cases) (12,13).

Magnetic resonance imaging (MRI) is well established for pre-operative staging of rectal cancer (14) as it has better soft-tissue contrast than CT allowing for higher resolution imaging of the layers of the bowel wall and its adjacent structures. The diagnostic performance of MRI and CT for LACC has been compared in numerous studies, MRI has been shown to be superior in defining T3 tumours with serosal involvement and T4 tumours as it has a higher specificity and lower false positives compared to those of CT (15-19) allowing for less over-staging. Combined with its known precision in detecting liver metastases and extramural vascular invasion (EMVI) MRI could become the most optimal abdominal staging method for patients with high risk colon cancer (18).

Molecular testing, especially for, microsatellite instability (MSI), *BRAF* and *KRAS* mutations, is currently routine practice in patients with locally advanced and/or metastatic colon cancer as it not only aids with prognostication, but also, helps guide treatment (8). MSI is a form of genetic instability owing to the deficiency of the DNA mismatch repair (MMR) mechanisms resulting in hypermutability. Those with MSI have a better prognosis than those with microsatellite stability (MSS), this is particularly important as 15–20% of stage II and III colon cancers are MMR-deficient or MSI (20). To date, *BRAF* mutations have no clear role in guiding treatment decisions, however, are useful in predicting outcomes, and while it has been shown that patients with *BRAF*-mutant metastatic colon cancer have significantly poor survival (21), its prognostic role in non-metastatic LACCs remains controversial, particularly amongst MSI *vs.* MSS tumours (22). Targeted therapy is generally given in conjunction with chemotherapy and

is largely guided by the tumour's *KRAS* mutation status. *KRAS* mutations predict resistance to epidermal growth factor receptor (EGFR) inhibitors such as cetuximab and panitumumab, resulting in their restricted use in only patients with *KRAS* wild-type tumours (23). Other targeted monoclonal antibodies include bevacizumab [active against vascular endothelial growth factor (VEGF)] and ramucirumab [active against vascular endothelial growth factor receptor (VEGFR)] (24).

The importance of pre-operative staging is to answer one main question—is the patient a candidate for a potentially extended R0 resection or not?

### Treatment strategies

In the elective setting, the NCCN outlines the management of resectable colon cancer based on the presence of obstructing symptoms. Non-obstructing cancers are treated with a colectomy with regional lymphadenectomy, whereas, for obstructed cancers temporary diversion is recommended either at the time of colectomy or before definitive surgery (8). Importantly, in emergent situations where a radical resection is not possible, or difficult to achieve, for example in patients who present with intestinal obstruction without tumour perforation or peritonitis, a defunctioning ostomy should be considered in lieu of resection the primary, this not only allows for decompression but also facilitates neoadjuvant therapies.

### NAC in LACC

Complete oncologic resection followed by adjuvant chemotherapy (AC) is the current standard treatment for patients with LACC, however, this approach may require extensive *en bloc* multivisceral resection to achieve negative microscopic margins (25). Despite this aggressive approach, the rate of R0 resections remains underwhelming, varying between 40–90% (25,26) with associated increased postoperative morbidity and mortality (26).

NAC is postulated to enhance tumour regression and aims to downstage tumours (27), improving resectability and promoting higher rates of local control hence, achieving more R0 resections (28–31). This has been proven to be effective in locally advanced oesophageal (32), gastric (33), rectal (34) and breast cancer (35).

To date NAC in LACC has been vastly understudied, however; based largely on emerging data from several phase II trials (36,37), the NCCN have added NAC as a

treatment option for patients with clinical T4b disease (8). *Table 1* summarises all published randomised control trials investigating NAC in LACC.

The FOxTROT Collaborative Group (36) investigated the feasibility, safety, and efficacy of preoperative chemotherapy for LACC. In this randomised control trial, 150 patients with radiologically staged locally advanced high risk T3 (with  $\geq 5$  mm invasion beyond the muscularis propria) or T4 tumours from multiple UK centres were randomly assigned either to 3 cycles of neoadjuvant FOLFOX (folinic acid, fluorouracil and oxaliplatin) followed by surgery with a subsequent 9 cycles as adjuvant therapy or up front oncological resection with a standard 12 cycles of adjuvant FOLFOX. *KRAS* testing was instituted shortly after the trial had commenced and aimed to randomly assign patients with *KRAS* wild-type tumours to receive panitumumab (6 weeks) or not, 46 (31%) of the 90 eligible patients received panitumumab. They reported that NAC resulted in significant downstaging compared with the postoperative group ( $P=0.04$ ), especially in those with apical node involvement ( $P<0.0001$ ) and exhibited two pathological complete responses. They also found resection margin involvement to be significantly lower in those treated with NAC ( $P=0.002$ ) and observed significant tumour regression grading ( $P=0.0001$ ) without incurring significant perioperative morbidity.

Jakobsen *et al.* (37) investigated whether NAC could convert high-risk patients (those requiring AC) to a low-risk (not requiring AC). Seventy-seven patients with histologically diagnosed adenocarcinoma, CT scan showing a high risk T3 or T4 tumour with no metastases on staging CT were divided into two groups according to mutational status (wild type *vs.* mutated + unknown) in this Danish phase II randomised control trial. Patients with *KRAS*, *BRAF*, *PIK3CA* mutation or unknown mutational status received three cycles of neoadjuvant CAPOX (capecitabine and oxaliplatin) while wild-type patients received the same chemotherapy supplemented with panitumumab. All patients then proceeded to oncological resection and were further stratified post histopathological analysis. Those who had high risk T3 tumours defined as having at least one of following factors: (I)  $<12$  lymph nodes in resection specimen, (II) poorly differentiated tumours, (III) vascular, lymphatic or perineural invasion or T4 tumours were deemed 'non-converters' and received a further five cycles of the CAPOX without panitumumab. The study's primary end point was 'converted' patients *i.e.*, those not fulfilling the criteria for AC and this cohort was offered

**Table 1** Published randomised control trials investigating NAC in LACC

	Study		
	FOxTROT (36), randomised phase III, 2012	Jakobsen <i>et al.</i> (37), randomized phase II, 2015	PRODIGE 22 (38), randomised phase II, 2020
Number of patients	150	77	104
Radiological inclusion criteria	High risk T3 or T4 tumour, N0–2, M0		High risk T3 or T4 tumour, N2, M0
Neoadjuvant group	FOLFOX (3 cycles)	CAPOX (3 cycles)— <i>KRAS</i> , <i>BRAF</i> , <i>PIK3CA</i> mutant tumours; CAPOX (3 cycles) + panitumumab	FOLFOX (4 cycles)
Control group	Immediate surgery	(3 cycles)— <i>KRAS</i> , <i>BRAF</i> , <i>PIK3CA</i> wild-type tumours	Immediate surgery
Adjuvant chemotherapy	NAC arm—FOLFOX (9 cycles); control arm—FOLFOX (12 cycles)	CAPOX (5 cycles)—‘non-converters’	NAC arm—FOLFOX (8 cycles); control arm—FOLFOX (12 cycles)
Primary outcome	Feasibility of NAC	Conversion from high risk to low risk	Tumour regression
NAC completed (%)	89%	83%	96%
Statistically significant difference in perioperative mortality or morbidity (NAC vs. control)	No	–	No
R0 resection (NAC vs. control)	96% vs. 80% (P=0.002)	–	94% vs. 98% (P=0.617)
Statistically significant tumour downstaging (NAC vs. control)	Yes	No (trend to downstaging)	Yes
Statistically significant histological tumour regression (NAC vs. control)	Yes	–	Yes
Complete histological response in NAC group	2	3	0

NAC, neoadjuvant chemotherapy; LACC, locally advanced colon cancer; FOLFOX, folinic acid, fluorouracil and oxaliplatin; CAPOX, capecitabine and oxaliplatin.

follow up only. The overall conversion rate from high risk patients to low risk patients was 42% in the wild-type group compared to 51% in patients with a mutation. Secondary end points were recurrence rate and disease-free survival (DFS). The group reported a cumulative recurrence rate in converted versus unconverted patients of 6% vs. 32% (P=0.005) with a 3-year DFS of 94% vs. 63% (P=0.005). Jakobsen *et al.* concluded that NAC is feasible in LACC and acknowledged that the study partly relies on an elimination of lymph node metastases and that conversion rates should be interpreted with caution as pre-operative CT may not show nodal involvement that may subsequently be found in the resection specimen.

A phase II multicentre French randomized controlled

trial (PRODIGE 22) (38) evaluated the efficacy and safety of NAC in patients with locally advanced non-metastatic colon cancer. One hundred and twenty patients with resectable high risk T3 or T4 tumour and/or N2 nodal involvement were randomised to receive either eight cycles of adjuvant FOLFOX after colectomy or four cycles neoadjuvant FOLFOX ± cetuximab (depending on *RAS* mutation status) followed by colectomy and subsequent eight more cycles of the same chemotherapy post operatively. Importantly, at interim analysis, the FOLFOX + cetuximab arm was ceased due to lack of efficacy and hence this arm was excluded from statistical analysis. While, of the 104 patients analysed, the group did not observe any major pathological response (TRG1) in the NAC arm they did find a significant

Table 2 Single arm prospective phase II trials

	Study	
	Liu <i>et al.</i> (39), single arm prospective phase II, 2016	Zhou <i>et al.</i> (40), single arm prospective phase II, 2016
Number of patients	47	23
Radiological inclusion criteria	High risk T3 or T4 tumour, N0–2, M0	T4N2M0
NAC	CAPOX: 2 cycles If no tumour regression after 2 cycles—patients proceeded to surgery If regression of tumour observed—patients received 1–2 more cycles of CAPOX	FOLFOXIRI: 4 cycles
Adjuvant chemotherapy	CAPOX: total of 8 cycles including neoadjuvant	FOLFOXIRI/CAPOX: 6 cycles
Primary outcome	Tumour response	Feasibility, safety, tolerance and efficacy
NAC completed	Average of 2.7 cycles, 89%	52%
NAC associated adverse events, grade 3 (%)	9%	57%
R0 resection	100%	87%
Radiological tumour response to NAC (%)	68%	91%
Pathological tumour regression grade	TRG >3 in 68%	Mandard TRG >4 in 74%
Complete histological response in NAC group	1	1

NAC, neoadjuvant chemotherapy; CAPOX, capecitabine and oxaliplatin; FOLFOXIRI, folinic acid, fluorouracil, oxaliplatin and irinotecan.

pathological regression 44% *vs.* 8%,  $P < 0.001$  in the NAC arm compared to the control arm with a trend to tumour downstaging without significant difference in overall mortality and morbidity rates.

Table 2 depicts two Chinese single arm phase II prospective trials (39,40) investigating the feasibility, safety and tumour response of NAC in LACC have also reported significant tumour regression and downstaging with acceptable toxicity and perioperative morbidity. Additionally, multiple retrospective propensity-score matched cohort analysis studies exploring patients with T4 colon cancer treated with NAC have shown significant radiological and pathological regression (41–43) with a higher 3-year overall survival (OS) (44).

In a recent presentation at the ESMO Congress 2019, the FOxTROT Collaborative Group presented an interim analysis of a further 1,053 patients across 98 hospitals in the UK, Denmark and Sweden (45). Of the 699 patients allocated to the NAC arm, 88% completed the three cycles of neoadjuvant FOLFOX and had marked histological downstaging after NAC with a lower pT and pN stage

( $P < 0.0001$  for both). A small subset of NAC arm patients displayed a complete (3.8%) and near-complete (4.6%) tumour regression. Serious perioperative complications, prolonged hospital stays and re-operation rates were lower in NAC group.

In summary, it appears that NAC is a safe, feasible and well tolerated therapy in LACC, current evidence, although still emerging, suggests NAC can cause significant tumour regression and downstaging with minimal adverse outcomes and perioperative morbidity.

### *NRT for LACC*

The role of NRT in LACC remains unclear and while there is ongoing research evaluating its safety and efficacy (46,47), there is relative paucity of definitive data supporting its use in this patient population. Theoretical benefits of NRT include downsizing and decreased risk of tumour cell shedding, making surgical outcomes more favourable in terms of achieving R0 resections. NRT also potentially carries a lower side effect profile and toxicity as healthy

**Table 3** Case series exploring use to neoadjuvant chemoradiotherapy in the treatment of LACC

Study	Type of study	Number of patients	Location of cancer	NAC	NRT (Gy/Fr)	R0 resection (%)	OS (%/year)	DFS (%/year)
Huang <i>et al.</i> , China, 2017 (50)	Retrospective cohort study	36	Any LACC	FOLFOX	45–50.4/25–28	31/34 (91.2)	88.7/2	73.6/2
Qui <i>et al.</i> , China, 2016 (51)	Prospective	21	Locally advanced sigmoid cancer	Capecitabine based	46–50/23–25	20/21 (95.2)	100.0/3	88.9/3
Cukier <i>et al.</i> , Canada, 2012 (52)	Retrospective cohort study	33	Any LACC	5-FU based	36–50.4/18–28	33/33 (100.0)	85.9/3	73.7/3

LACC, locally advanced colon cancer; NAC, neoadjuvant chemotherapy; NRT, neoadjuvant radiotherapy; OS, overall survival; DFS, disease-free survival; FOLFOX, folinic acid, fluorouracil and oxaliplatin; 5-FU, 5-fluorouracil.

tissues with preserved tissue oxygenation and blood supply allow for better penetration to neoplastic tissue compared to fibrosed post-operative tissue. There is however, emerging evidence validating these theoretical benefits.

Krishnamurty *et al.* (48) conducted a cohort analysis to determine the outcomes of NRT on patients with non-metastatic T4 colon cancer. Patients were divided into two groups, those who received NRT and those who did not, all patients proceeded to oncological resections with the primary outcomes being R0 resection and OS. Of the 131 patients included in the study 23 patients (17.4%) received NRT. They found a non-statistically significant improvement in R0 resection rate and local recurrence with a median follow up for 52.6 months. There was, however, a statistically significant difference in tumour downstaging ( $P=0.007$ ) and an improved 5-year OS ( $P=0.03$ ) in the NRT cohort. There were several limitations to this study, including small sample size, selection bias, and although pre-treatment factors in both the two cohorts were similar, there was inconsistency in radiation technique/dose and chemotherapy regimen amongst the groups. Additionally, 91% of those in the NRT group received NAC compared to 3% of those in the non-NRT group which may further confound results.

A larger 2019 study by Hawkins and colleagues (49) analysed the National Cancer Database (United States of America and Puerto Rico) for use of NRT in patients with stage T4 LACC. The 15,207 patients with clinical T4 disease who underwent resection were included in the study of which 195 patients (1.3%) underwent NRT. The team reported that NRT was associated with a non-statistically significant improvement in R0 resection rates but an improvement in 5-year OS ( $P<0.001$ ). Furthermore, a subgroup analysis of only patients with clinical T4b

disease revealed that this group was more likely to undergo NRT with an improved 5-year OS ( $P=0.002$ ). A major limitation of this study is incomplete data collection in terms of preoperative staging, tumour location, organs involved in either tumour extension or multivisceral resection, radiation dosing, fields, and side effects. As there was no randomisation for consideration of NRT, significant selection bias may exist. Additionally, a key outcome of NRT is local recurrence which was not captured by this database.

### *Neoadjuvant chemoradiotherapy for LACC*

The use of combined neoadjuvant chemoradiotherapy for LACC has only been reported in case reports and three small case series (50–52). These studies (Table 3), while severely limited by sample size and length of follow up, reported encouragingly high rates of achieving R0 resection and pathological complete response.

### *Surgical treatment*

LACC presents a surgical challenge as the tumour, especially T4 tumours, can extend, adhere and even invade into adjacent organs. These adhesions present an exceptionally high risk of being malignant, this combined with the fact that intraoperative assessment of nature of adhesions is often inaccurate (53), guidelines recommend *en bloc* multi-visceral resections for treatment of these tumours. Multiple studies have validated extended resections improve the likelihood of negative resection margins and are associated with a better improved OS (8,54,55).

The most frequent organs involved are the bladder and loops of small bowel (25,53,56), however, dependant on the

location of the tumour, it may also invade the abdominal wall, pancreaticoduodenal region, liver, stomach, spleen and/or urinary tract (kidney, ureters).

#### ***Anterior invasion (small bowel, bladder, prostate, seminal vesicles, vagina)***

Tumour invasion of small bowel loops can be solved by an *en bloc* enterectomy while invasion of other parts of colon may require extended colectomy or even a subtotal colectomy.

In cases where the tumour has invaded into the bladder, without distant metastases, an *en bloc* resection would require a full thickness excision of the bladder wall with a 2–3 cm margin (57-59). While primary reconstruction of the bladder is achievable in the majority of cases, the decision to perform total rather than partial cystectomy should be based on the anatomic location of the tumour, with tumours invading the dome of the bladder, as is the case with most LACCs, necessitating only a partial cystectomy ensuring adequate radial margins macroscopically (60) as the local recurrence and survival rates of both procedures seems to be comparable given negative resection margins (61).

#### ***Superior invasion (stomach, duodenum, pancreas, gallbladder, spleen)***

An *en-bloc* resection of a T4 transverse colon cancer that invades into the stomach involves either a wedge resection of the greater curvature or a distal gastrectomy dependent on level of invasion (62). An invasive splenic flexure cancer may require a splenectomy or even a splenopancreatectomy, if the tail of the pancreas is involved (63), whereas, an invasive hepatic flexure cancer likely necessitates a cholecystectomy and a wedge or segmental liver resection (62,64). Right sided colon cancers can invade into duodenum and/or head of pancreas, and as such can be surgically challenging. Limited duodenal invasion generally requires a partial duodenectomy with primary suture closure, if possible, or a duodenojejunostomy in defect is too large (65). When the pancreatic head is involved, selected patients may undergo a curative pancreaticoduodenectomy (66).

#### ***Posterior invasion (major vessels, kidneys, ureters)***

Tumour involving superior mesenteric or common iliac artery are commonly deemed unresectable (67), however,

with recent advances in vascular interposition grafts, femoral-femoral bypasses and primary anastomoses this is no longer the case (68). Right or left T4 colon cancers can invade the kidney and/or the ureter which can be solved with an *en bloc* nephrectomy and/or ureterectomy (69,70). If the contralateral kidney has abnormal function, an uretero-ureteral anastomosis may be possible (71), however, if there is adequate ureteric length remaining and a nephrectomy was not indicated in the oncological resection, reimplantation of the ureter into the bladder via a Boari flap with or without a psoas hitch can maintain baseline renal function (71,72).

#### ***Peritoneal invasion***

For selected patients with low volume peritoneal metastasis, the NCCN recommend consideration of cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC) (8). This is largely based on the results of a randomised control trial by Verwaal *et al.* (73) that evaluated systemic 5-fluorouracil (5-FU) alone versus cytoreduction and HIPEC with mitomycin C, the team demonstrated a doubling of survival (22.3 *vs.* 12.6 months) in those that underwent cytoreduction and HIPEC compared to systemic therapy alone. The controversial PRODIGE 7 trial (74) compared cytoreductive surgery plus HIPEC and perioperative oxaliplatin against cytoreductive surgery alone, and while the team did not meet its primary endpoint of OS with the addition of perioperative oxaliplatin to cytoreductive surgery and HIPEC, they did find while that cytoreductive surgery alone showed satisfactory OS, the addition of HIPEC may potentially delay initial recurrence.

#### ***Adjuvant radiotherapy for LACC***

The role of adjuvant radiotherapy in LACC is poorly defined, to date, there has been only one randomized control trial (Intergroup-0130) (47) which sought to evaluate the role of AC and radiotherapy compared with AC alone in patients with LACC. The trial was unfortunately terminated prematurely due to poor accrual, however, the study did show 5-year OS and DFS were comparable in both groups with patients in the chemoradiotherapy arm experiencing higher toxicity. A recent sizable propensity score matched retrospective cohort analysis by Sebastian *et al.* (75) found no statistically significant difference in OS between patients with T4 colon cancer treated with or without adjuvant radiation but highlighted that it may be

useful in those with T4b lesions and/or positive margins following resection, this was further echoed by smaller retrospective observational studies (46,76).

## Conclusions

Even with the considerable advancements in imaging modalities of late in preoperative staging, accurate diagnosis of T4 colon cancer remains a difficult task, this is due to the significant percentage of cases that present with acute bowel obstruction or tumour perforation and the inability of these imaging modalities to accurately predict the true level of malignant invasion. There is increasing literature defining the role of NAC and radiotherapy to improve R0 resections and survival in T4 colon cancer however, is not yet widely recommended by either NCCN or ESMO guidelines. Extended multi-visceral *en bloc* resections are imperative in T4 colon cancers and carry an acceptable postoperative morbidity and mortality as achieving R0 resections may offer the chance for a cure.

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