NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **IP1724 Low-energy contact X-ray brachytherapy (the Papillon technique) for locally advanced rectal cancer**

Your information

Name:	Arthur Sun Myint
Job title:	Lead Clinician (Papillon)
Organisation:	Clatterbridge Centre for Oncology
Email address:	[redacted]
Professional organisation or society membership/affiliation:	The Royal College of Radiologists (RCR) Association of Coloproctology of Great Britain and Ireland (ACPGBI) European Society of Radiotherapy and Oncology (ESTRO) International Contact Radiotherapy Network (ICONE)
Nominated/ratified by (if applicable):	NA
Registration number (e.g. GMC, NMC, HCPC)	2293365

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

☐ Please tick this box if you would like to receive information about other NICE topics.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice.

☒ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? – Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?	My international peers including NICE (2015 & 2019) regards me as one of the world opinion leaders in Contact X-ray Brachytherapy [CXB] (Papillon) for rectal cancer. I introduced CXB technology into the UK in 1993 following my visit to Lyon with my team in 19992. I set up the first Papillon centre at Clatterbridge and offer this service to suitable patients with rectal cancer. The referrals has increased year on year and we are now treating over 200 patients per year. I have treated over 3000 patients in the past 31 years which is the world largest cohort ever treated by this technology. Prof Papillon himself has treated just over 300 patients in his lifetime (1914-1993) and Prof Jean Pierre Gerard (1944-) over 500 patients. I organise training for other UK and international centres interested to setup CXB technology together with my mentor Prof Jean Pierre Gerard (who has now retired from clinical practice since Dec 2023), We have trained and set up 4 Papillon centres in the UK and 10 in the Europe.

	− Is this procedure/technology performed/used by clinicians in specialities other than your own? − If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	Yes. There are now 4 centres in the UK (Clatterbridge (1993); Hull (2011), Nottingham (2014) and Guildford (2014). Between our 4 centres, we treat approximately 500 out of potential 2000 patients a year who are suitable for CXB. Welsh Government has commissioned HTA for Papillon to set up a new facility for Wales as all Welsh patients has to travel (6-8 hours) to the UK for their treatment. HTA review is positive and it is highly likely that the first Welsh centre paid by the Welsh government will be in Swansea from later this year (HTA report 2024). There are few other UK centres trained and hoping to start Papillon facilities in London (Royal Free and The Royal London), Ipswich & Colchester, and the Royal Devon and Exeter. This procedure can be used to treat skin cancers and IORT for Breast (both centres in France) I have no experience of this procedure use in either skin or breast. However, Royal Liverpool hospital breast surgeons are keen to set up IORT for post lumpectomy screen detected patients. Most UK radiotherapy centres has superficial x-rays ortho voltage machines for skin treatments (some very old and needs replacement). The new Papillon Plus machine can treat both rectum and skin with substantial cost savings to the NHS. Centres who wish to start Papillon facilities for rectum will be able to treat their skin patients using the same machine and vice versa. I helped write RCR (2024), GEC-ESTRO (2022),and ACPGBI guidelines for patient selection (Colorectal Disease 2017) The new Papillon Plus will have a separate machine for Breast IORT (similar to Zeiss machine used in TARGIT trial [BMJ 2022])
2	− Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure (Yes, systemic review/meta-analysis due for publication shortly). I have done research on this procedure in laboratory settings (e.g. device-related research) (No, but planning to do one shortly with Prof Tim Maughan and Prof Christian Ottensmeier from The University of Liverpool). I have done clinical research on this procedure involving patients or healthy volunteers (Yes, OPERA). I have published this research (Yes, OPERA Trial 2023(GI Lancet), 2025 (Annals of Oncology).

		I have been involved in research on this procedure (OPERA- phase 3 randomised trial- level 1b). Other (We are planning to set up another randomised trial on CXB in the UK. External beam combining with immunotherapy and CXB called OPERA-D. NIHR funding is in place for this type of trial at the Royal Free Hospital in London (2024).
3	Does the title adequately reflect the procedure? How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	No. Definition of locally advance rectal cancer can be difficult and confusing. Both T3 and T4 are defined by NICE is locally advanced. Most clinicians will regard locally advanced rectal cancer as only when CRM involved (+ive) or cT4 (involve other organs or adjacent structures) with N2 disease. This procedure/technology [Papillon (CXB)] is not usually offer to patients with locally advanced rectal cancer (cT4/cN2/ CRM +ive) as the initial treatment. However, it can be offer as a boost after External Beam Chemo Radiotherapy Therapy (EBCRT)) for patient with locally advanced rectal cancer which is the standard of care. In those patients who respond to TNT (Total Neoadjuvant Therapy) resulting in downsizing and down staging of tumour with minimal residual disease (<3cm, yT1or yT2), CXB can be offered as an option. This procedure therefore, provide an innovative approach for patients with locally advance cancer who are not suitable for surgery or those vehemently refusing surgery (Patient's choice). Established practice and no longer new. (No) **A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy. Yes. Existing procedure IPG 532 (2015)- evaluated the efficacy and safety of CXB for patients with early rectal cancer not suitable for surgery. Definitely novel and of uncertain safety and efficacy. No- (IPG 532 has evaluated the safety and efficacy of CXB) The first in a new class of procedure.(No) It has been used in Europe and USA for more than 80 and 50 years respectively.

4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	4.1 Yes. This procedure has a potential to use as an alternative procedure to replace current SOC, which is TME or local excision for early rectal cancer cT1/ cT2 cN0 (NICE guidance 2022) as not all patients are suitable or agreeable to have extirpative surgery and a stoma. 4.2 CXB procedure can also be used as an addition to EBCRT (SOC) for more advanced rectal cancers (cT3a-b /cN1). Adding CXB has shown in a randomised phase 3 multi-centre trial to improve local control, reduce regrowth and improve organ preservation rates as in OPERA trial (GI Lancet 2023, Annals of Oncology 2025).
5	Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	Yes, the new Papillon Plus machine (Ariane / Clerad©) uses modern technology unlike RT50 Philip or Papillon 50. The treatment delivery is quick (just over 2 minutes) and treatment application is much more comfortable to the patients. There are many features to improve security and safety of the treatment delivery with the new Papillon Plus machine. It is a portable and battery operated low energy (50 kVp) robust machine. It uses high quality endoscopic image guided system for accuracy and precision of treatment delivery. All images can be captured on the system before and after treatment for safety checks. All pictures are stored electronically on the machine which can be transferred on to our hospital system for data recording and facilitates sharing with other referring centres. We can also review and analysis the images for research and training later. Yes. • International Contact Radiotherapy Network (ICONE) group has published a phase 3 European randomised trial in GI Lancet (3 years Feb 2023); Annals of Oncology (5 years Oct 2024(online), Feb 2025). • Safety and feasibility of surgical salvage for patients with local failures in OPERA trial was published in Colorectal Disease (Sept 2023). • Welsh Health Technology Assessment (HTA) was published online (Jan 2024) and a review manuscript was published in Colorectal Disease (2024). • Systemic review and Meta-analysis on CXB has been carried out and manuscript will be submitted to EJSO (European Journal of Surgical Oncology) for consideration of publication (March/April 2025)

Current management

6	Please describe the current standard of care that is used in the NHS.	6.1 SOC for early rectal cancer (cT1/cT2/cN0)– currently is either TME with stoma or local excision. For both procedures patients' need general anaesthesia and hospital in patient stay. There is surgical mortality from 10 to 25% (30 days) and morbidity 30-50%(in older patients who are over 80 years patient with multiple comorbidities) 6.2 SOC for advanced rectal cancers (cT4- with CRM + and cN2) preoperative chemo-radiotherapy followed by TME surgery with surgical mortality, morbidities and stoma in 60% of cases. Needs general anaesthesia, 6-8 hours operation and hospital stay up to 7-10 days depending on age and comorbidities. The majority of patients with rectal cancer in the UK are older (above 70 years) with multiple co-morbidities (CRUK data). TME surgery has high cost to the NHS and cancer targets put additional pressure on surgical waiting list.
7	Are you aware of any other competing or alternative procedure/technology available to the NHS, which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	Yes. External beam short course or EBCRT (long course) are offer to many patients with early rectal cancer as they are now refusing surgery to avoid a stoma. Those who achieve clinical complete response (cCR) or clinical near complete response (ncCR) are offer Watch and wait policy with local regrowth 25-30% needing surgery resulting in organ preservation rates of less than 50%. All competing procedure/technologies use external beam radiotherapy with daily attendance to hospital for either 5 days or 5 weeks with or without chemotherapy. Organ preservation achieve is usually less than 50%.

		The available procedure/technology uses high-energy external beam radiotherapy usually combined with chemotherapy. There is associated mortality of 1-2% and there are many side effects to bowels, bladder, skin, sexual function. It require daily attendances of up to 30 days and occasional hospitalisation (for grade 3-4 toxicity). QOL following treatment in older patients can be poor and worse if they needed surgery with added surgical mortality and complications.

4

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	• Papillon treatment involves three outpatient visits each lasting between 30-60 minutes. • No GA is necessary • No risk of mortality or morbidity • No hospital admission for inpatient stay • No need for a stoma • Ambulatory short day case treatment • Acceptable toxicity and safety (HTA Wales (2025);NICE IPG 532 (2015) • High chance of organ preservation over 80%(OPERA phase 3 randomised trial) • Low cost to NHS (HTA Wales report)
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Older and frail patients not suitable for surgery(IPG532) but this option was not included in the main NICE recommendations for early rectal cancer treatment (2020) Younger or older fit patient suitable for surgery with early or more advance rectal cancer wishing to avoid surgery and a stoma (patients' choice). We now have published phase 3 randomised trial evidence OPERA to support this (Level 1b).
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Yes. This procedure has the potential to change current pathway, improve outcomes, and improve QOL for patients suitable for surgery with benefits to Health care system (HTA evaluation, Wales 2024). When a patient refused surgery, the standard of care is to offer EBCRT. Approximately up to 60% can achieve clinical complete response (cCR) and the patients can adopt a watch & wait strategy with deferral of surgery. Unfortunately about 25-30% of patients who had achieved cCR will develop local regrowth needing salvage surgery. The ultimate organ preservation will be less than 50%. Randomised phase 3 OPERA trial has clearly shown benefit of adding CXB to EBCRT will significantly improve clinical outcomes (GI Lancet (2023); Annals of Oncology (2025). Papillon can be deliver as three two weekly outpatient visits without a need for extirpative surgery or a stoma. Substantive cost saving to the NHS has been assessed by Welsh HTA(2024)

11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	The majority of large UK radiotherapy centres will have brachytherapy facility. We can set up Papillon facilities in the existing UK radiotherapy departments with brachytherapy facilities (e.g. Hull, Guildford and Nottingham). No shielding or special housing unit is necessary, as the Papillon is a low energy (50KVp) machine unlike HDR (radioactive Iridium source). Papillon Plus machine is relatively small (size of Ultrasound machine) and is mobile. Can be parked or placed and stored in a relatively small room. No special bunker or radiation protected room necessary.
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	We regularly organise two Papillon training courses at Clatterbridge a year for new centres hoping to set up Papillon facilities since 2010. It is two days course and approximately 10-15 delegates attend from 3-5 different UK and international centres. Next course is on 26th -27th March and 24th -25th September 2025. Delegates comes back for 3-5 days hands-on training. We go to their centres when they acquired CXB facility to start at their own centre. We help to initiate the treatment until they are confident to offer CXB treatment independently. We have helped setup 4 CXB centres in the UK and 10 in Europe which include four centres in France (2009- 2024), Uppsala (2014), Amsterdam (2016), Tenerife (2019), Zurich (2018), Eindhoven (2019), and Stockholm (2025). One centre in Wales and two centres in USA will be starting shortly. We have annual meetings with all Papillon facilities in UK and Europe where we present, share our experiences. We collaborate in research projects and contribute to the trials.

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events.	NICE has reviewed safety of CXB in detail for their IPG532 (2015) recommendation. In addition, NICE surveyed 61 patients in 2019. The majority do not report significant major side effects (manuscript in preparation). Papillon treatment is very well tolerated. 1. No procedure related mortality reported unlike surgery. 2. Rectal bleeding G1 or G2 occurs in 63% of cases who had Papillon compared to 12% for EBCRT. Bleeding usually settles after 6-12 months. Argon beam is necessary in 10% of cases with persistent bleeding usually in patients who are on Blood thinners. 3. Rectal ulceration occurs in 40% of cases mostly superficial and asymptomatic. Ulcer usually heals after 6-12 months. No intervention is necessary. 4. No reports of surgical intervention needed for any Papillon related adverse events.

14	Please list the key efficacy outcomes for this procedure/technology?	Published randomised phase 3 OPERA trial confirmed 1. Improved organ preservation of 53 % for EBCRT (Arm A-SOC) vs 93% with EBCRT +CXB(Arm B-experimental) at 5 years 2. Improve cCR 64% (Arm A) vs 92% (Arm B) 3. Reduces local regrowth 37% (Arm A) vs 18% (Arm B) [5 year]
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	The safety of CXB procedure was evaluated in depth by NICE (IPG532). NICE accepted that there are no safety issues with CXB both for patients not suitable or suitable for surgery (2015). Data was considered sufficient to support efficacy in patients unfit for surgery but recommend a randomised trial for patient fit for surgery. Randomised phase 3 multi-centre trial OPERA confirmed efficacy for fit patients (PS0-1) with cT2 /cT3a-b/ cN0/cN1 (Dukes C) <5cm in size (GI Lancet [2023], Annals of Oncology [2025])
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Surgeons are concern about safety and efficacy of surgical salvage for local failures after CXB. The data on safety and efficacy for patients with local failures in OPERA trial published in Colorectal Disease (Sun Myint, 2023) confirmed most failures were salvage with over 90% R0 resection rate. There were no unsalvageable recurrences reported after CXB failure.
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Most or all district general hospitals. X A minority of hospitals, but at least 10 in the UK.** (we just need another <5 new centres in the UK) Fewer than 10 specialist centres in the UK. Cannot predict at present.

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this	1. A phase III randomized trial on the addition of a contact x-ray brachytherapy boost to

	procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	standard neoadjuvant chemo-radiotherapy for organ preservation in early rectal adenocarcinoma: 5 year results of the OPERA trial D. Baron, T. Pace Loscos, R. Schiappa et al. Annals of Oncology.2025; 36(2): 208-215 https://doi.org/10.1016/j.annonc.2024.10.827. 2. HTW. Low Energy Contact X-Ray Brachytherapy (CXB) for the Treatment of Early-Stage Rectal Cancer. 2023. Health Technology Wales. Accessed January 24, 2024. https://healthtechnology. wales/ reports-guidance/low-energy-contact-x-ray-brachytherapy-cxb/ 3. Stewart AJ, Van Limbergen EJ, Gerard JP, Appelt AL, Verhaegen F, Berbee M, et al. GEC ESTRO ACROP consensus recommendations for contact brachytherapy for rectal cancer. Clin Transl Radiat Oncol. 2022;33:15–22. https://doi.org/10.1016/j.ctro.2021.12. 004 4. Low energy contact X-ray brachytherapy for treatment of rectal cancer: a health technology Colorectal Disease appraisal by Health Technology Wales Hayley Bennett, Christopher Rao, Leona Batten et al. Colorectal Disease. 2024; 26:1053–1058. DOI: 10.1111/codi.16935 5. The safety and efficacy of total mesorectal excision (TME)surgery following dose-escalation: Surgical outcomes from the organ preservation in early rectal adenocarcinoma(OPERA) trial, a European multicentre phase 3 randomised trial (NCT02505750 A Sun Myint, C Rao, N Barbet, et al. Colorectal Disease. 2023;25:2160–2169 DOI: 10.1111/codi.16773

		6, Contact X-ray Brachytherapy in Rectal Cancer: A Systematic Review and Meta-Analysis Simon Powell, James Watt, Chris Rao et al. (submitted)
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	1. TRISOR trial (France) In locally advanced rectal cancer TNT with FOLFIRINOX +EBCRT +/- CXB (Funding approved and started) 2, OPPAX (Netherlands) small residual tumour following EBCRT or SCRT. Randomised to continue Watch and wait Vs CXB (Feasibility phase) ongoing 3. CORRECT (Sweden) cT2cT3a-b/cN0-cN1 <5cm. Randomised between EBCRT +CXB Vs SCRT +CXB Funding approved starting shortly 4. OPERA-D Immunotherapy + CXB (UK) (phase 2 feasibility progressing to Phase 3 randomised (Work in progress). 5. STAR TREC 3 (Netherlands) 3 arms Funding approved Ongoing 5x5 + CXB (boost) Vs 5x5 EBRT(boost) Vs 5x5 +CAPOX x3
20	Please list any other data (published and/or unpublished) that you would like to share.	See above CXB systemic review & meta-analysis (unpublished yet)

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	There are 14000 new patients diagnosed with rectal cancer each year in the UK. The number of patients diagnosed with stage I or II has increased from 35% (2016-17) to 38% (2020-21) due to Bowel Cancer Screening (BCS) started in 2006 in the UK. In addition, the number of patients having surgery has dropped in the same period from 54% to 47% [NBOCA 2022]. Therefore, there are approximately 5000 patient with rectal cancer suitable for part of their treatment with

		CXB. However, the majority of these patients will end up having surgery either TME or Local excision as recommended by their surgeon and approved by their local MDT (NICE guidance, 2022). However, increasingly number of patients are reluctant to accept surgery, as they are stoma phobic. They wish to maintain their QOL avoid distress of going through the trauma of surgery with loss of income due to days of absence from work. The patients should be given a choice as per 'Best practice guidelines' published by General Medical Council on Consent and shared decision making (Nov, 2020). There are potentially 2000 (1400 cT1/cT2/cN0) patients suitable for CXB but not offered at present as there were no published guidelines by NICE. At present, we only treat approximately 500 patients between 4 UK Papillon centres.
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	All these has been assessed in a randomised trial OPERA. We have updated and published our 5 year results with 3-year minimum follow up. Beneficial outcome measures: Short term 1. Clinical complete response (6 months) 2. Regrowth (3 years) 3. QOL & PROMS (3,6, 12 and 24months) Long term 1. Organ preservation rate (3 years) 2. TME free survival (3 years) 3. Surgical salvage rate (3 years) Adverse outcome measures: Short term 1. Unsalvageable regrowth

		Long term 1. Bleeding 2. Stoma rate

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	Papillon has been in clinical use for over 90 years around the world (Germany, France and USA). Papillon was introduced in the UK and first facility started at Clatterbridge in 1993. We have treated nearly 3000 patient over the past 30 years. This is the world largest cohort ever treated by this technique. Lyon 96-02 was the first randomised trial to evaluate Papillon (CXB) efficacy published in JCO over 20 years ago. NICE used this data to recommend CXB for patients with early rectal cancer not suitable for surgery (IPG 532; 2015). NICE reviewed and accepted that data on safety of this procedure was adequate for both patients unsuitable and suitable for surgery. However, they recommend a randomised trial to evaluate the efficacy for patients fit for surgery. We set up an OPERA trial to evaluate efficacy in patients fit and suitable for surgery. The results published in GI Lancet (2023) an Annals of Oncology (2025) on 141 evaluable patients with 38.2 and 61.2 months follow up, respectively. Organ preservation at 5year was 93% vs 53% for (cT2/cT3a-b / cN0/cN1) rectal cancer <3cm ((HR 0·07, 95% CI 0·01–0·57; p=0·012). This was a confirmatory trial for Papillon efficacy to support Lyon 896-02 trial. Published OPERA phase 3 randomised trial has clearly shown that addition of CXB improve organ preservation compared to EBCRT [SOC] (Level 1b). • Welsh HTA evaluation on cost effectiveness of CXB was positive (HTA 2024). CXB was estimated to improve QALYs as part of a watch and wait strategy for adults with T2–3b, N0–1, M0 rectal cancer, who are fit enough for surgery, at a higher cost than the comparator. The ICER of £4,463 per QALY gained indicates that CXB may be cost effective compared with external beam boost. • We have carried out systemic review. Our literature search identified 973 studies, of which 48 studies encompassing 5,447 patients met the predefined inclusion and exclusion criteria and were included in the meta-analysis. Pooled estimates of outcomes were as follows: complete Clinical Response rate =81% (95% Confidence interval (95%

		CI 75-87%), local recurrence =15% (95% CI 12-18%), salvage surgery =14% (95% CI 11- 18%) and long-term disease control. Post-salvage surgery =88% (95% CI 78-96%) respectively. This is a level 1a evidence for Papillon and we hope this will become a standard of care for patients with cT2/cT3a-b/cN0/cN1 (Dukes C) who are fit for surgery but wish to avoid a stoma (Level 1a). Finally, We need to get the definition for locally advanced rectal cancer right for this review. Rectal cancer should be divided into 3 categories as recommended in the MERCURY trial (2005). 1.The good (cT1/cT2/cN0) Suitable for CXB 2. The bad (cT3a-b/cN0/cN1) Suitable for CXB (OPERA trial) 3. The ugly (cT3 c-d [CRM involve] /cT4 / cN4. Selected patients for CXB (responders) (unfit/ vehemently refusing surgery) Papillon is not suitable for the ugly advanced (cT4cN2, CRM [+]) rectal cancers. However, there are small number of patients with ugly rectal cancer who respond well to TNT and EBCRT with significant down staging (approx. 10-25%). They are uncommon but in these selected patients (~20%) CXB can be offered as an option after MDT discussion. CXB can improve local control and reduce local regrowth, if the patients are not fit for surgery or vehemently refusing surgery (patients' choice). The French investigators are evaluation Locally advanced rectal cancer with intensive chemo using FLOFIRINOX 6cycles followed by EBCRT +/_ CXB. Funding by French research authority has funding approved and this trial has started last year. NB: I strongly advise to discuss fully on definition of locally advanced rectal cancer and to modify the title for this review accordingly. Happy to help with discussions.

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.	None		
Choose an item.			
Choose an item.			

X I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Arthur Sun Myint**
Dated:	**10 February 2025**