Optimal Timing Between Total Neoadjuvant Therapy and Surgery for Patients with Rectal Adenocarcinoma

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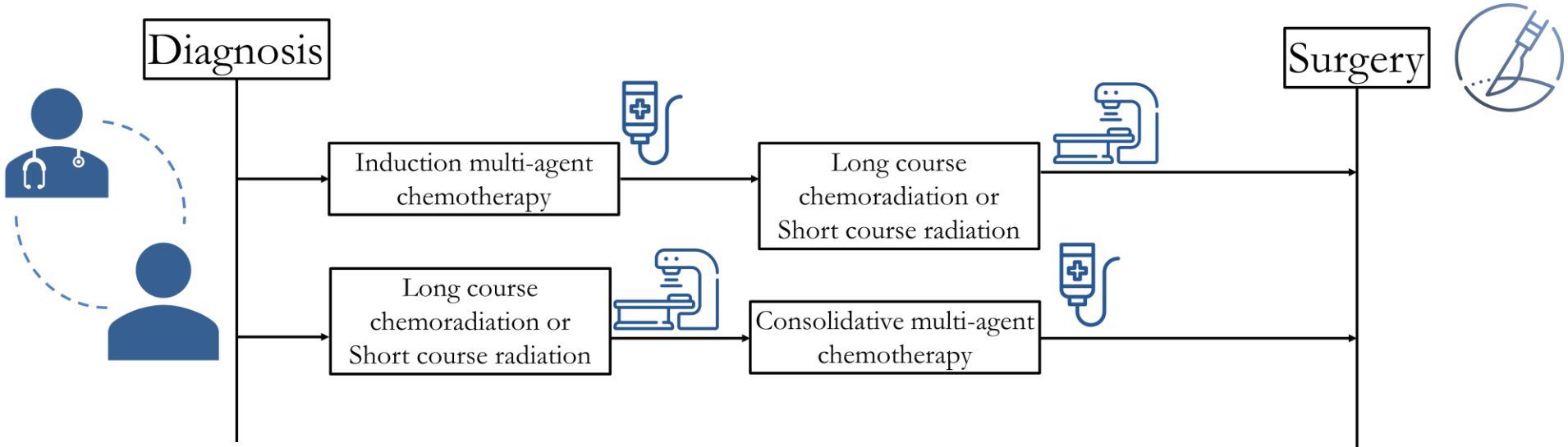
Introduction

Total neoadjuvant therapy (TNT)



Randomized Phase II Trial of Chemoradiotherapy Plus Induction or Consolidation Chemotherapy as Total Neoadjuvant Therapy for Locally Advanced Rectal Cancer: CAO/ARO/AIO-12

Emmanouil Fokas, MD, DPhil[1,2,3,4]; Michael Allgäuer, MD[5]; Bülent Polat, MD[6]; Gunther Klautke, MD[7]; Gerhard G. Grabenbauer, MD[8]; Rainer Fietkau, MD[9]; Thomas Kuhnt, MD[10]; Ludger Staib, MD[11]; Thomas Brunner, MD[12,13]; Anca-Ligia Grosu, MD[12]; Wolff Schmiegel, PhD, MD[14]; Lutz Jacobasch, MD[15]; Jürgen Weitz, MD[2,16,17]; Gunnar Folprecht, MD[2,16,17]; Anke Schlenska-Lange, MD[2]; Michael Flentje, MD[6]; Christoph-Thomas Germer, PhD[6]; Robert Grützmann, MD[9]; Matthias Schwarzbach, MD[18]; Vittorio Paolucci, MD[19]; Wolf O. Bechstein, MD[1]; Tim Friede, PhD[20]; Michael Ghadimi, MD[20]; Ralf-Dieter Hofheinz, MD[21]; and Claus Rödel, MD[1,2,3,4]; on behalf of the German Rectal Cancer Study Group

Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial

Renu R Bahadoer, Esmée A Dijkstra*, Boudewijn van Etten†, Corrie A M Marijnen†, Hein Putter, Elma Meershoek-Klein Kranenbarg, Annet G H Roodvoets, Iris D Nagtegaal, Regina G H Beets-Tan, Lennart K Blomqvist, Tone Fokstuen, Albert J ten Tije, Jaume Capdevila, Mathijs P Hendriks, Ibrahim Edhemovic, Andrés Cervantes, Per J Nilsson†‡, Bengt Glimelius†‡, Cornelis J H van de Velde†‡, Geke A P Hospers†‡, and the RAPIDO collaborative investigators§*

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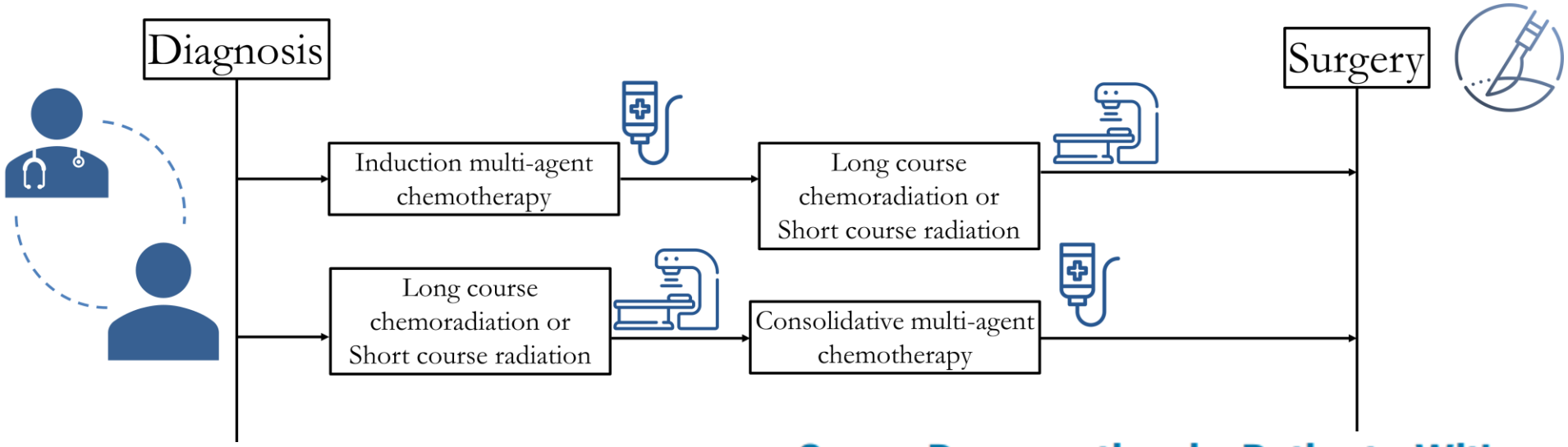

Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial

*Thierry Conroy, Jean-François Bosset, Pierre-Luc Etienne, Emmanuel Rio, Éric François, Nathalie Mesgouez-Nebout, Véronique Vendrely, Xavier Artignan, Olivier Bouché, Dany Gargot, Valérie Boige, Nathalie Bonichon-Lamichhane, Christophe Louvet, Clotilde Morand, Christelle de la Fouchardière, Najib Lamfichekh, Béata Juzyna, Claire Jouffroy-Zeller, Eric Rullier, Frédéric Marchal, Sophie Gourgou, Florence Castan, Christophe Borg, on behalf of the Unicancer Gastrointestinal Group and Partenariat de Recherche en Oncologie Digestive (PRODIGE) Group**

Organ Preservation in Patients With Rectal Adenocarcinoma Treated With Total Neoadjuvant Therapy

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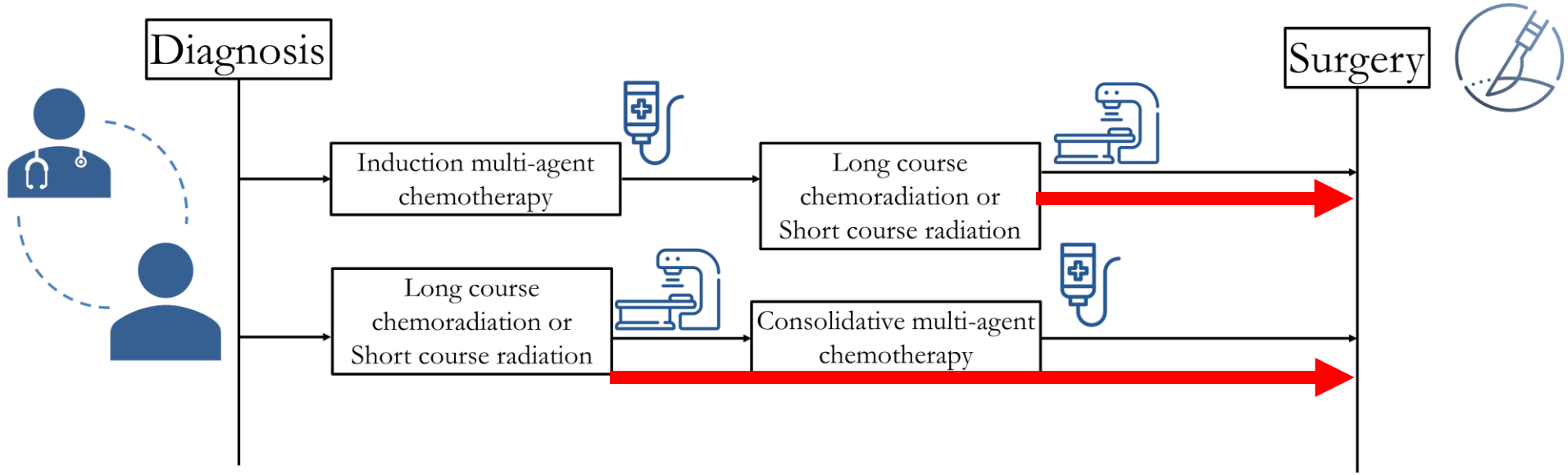
Introduction

Total neoadjuvant therapy (TNT)



Optimal fractionation of preoperative radiotherapy and timing to surgery for rectal cancer (Stockholm III): a multicentre, randomised, non-blinded, phase 3, non-inferiority trial

Johan Erlandsson, Torbjörn Holm, David Pettersson, Åke Berglund, Björn Cedermark, Calin Radu, Hemming Johansson, Mikael Machado, Fredrik Hjern, Olof Hallböök, Ingvar Syk, Bengt Glimelius, Anna Martling

Effect of Interval (7 or 11 weeks) Between Neoadjuvant Radiochemotherapy and Surgery on Complete Pathologic Response in Rectal Cancer: A Multicenter, Randomized, Controlled Trial (GRECCAR-6)

Jérémie H. Lefevre, Laurent Mineur, Salma Kotti, Eric Rullier, Philippe Rouanet, Cécile de Chaisemartin, Bernard Meunier, Jafari Mehrdad, Eddy Cotte, Jérome Desrame, Mehdi Karoui, Stéphane Benoist, Sylvain Kirzin, Anne Berger, Yves Panis, Guillaume Piessen, Alain Saudemont, Michel Prudhomme, Frédérique Peschaud, Anne Dubois, Jérome Loriau, Jean-Jacques Tuech, Guillaume Meurette, Renato Lupinacci, Nicolas Goasgen, Yann Parc, Tabassome Simon, and Emmanuel Tiret

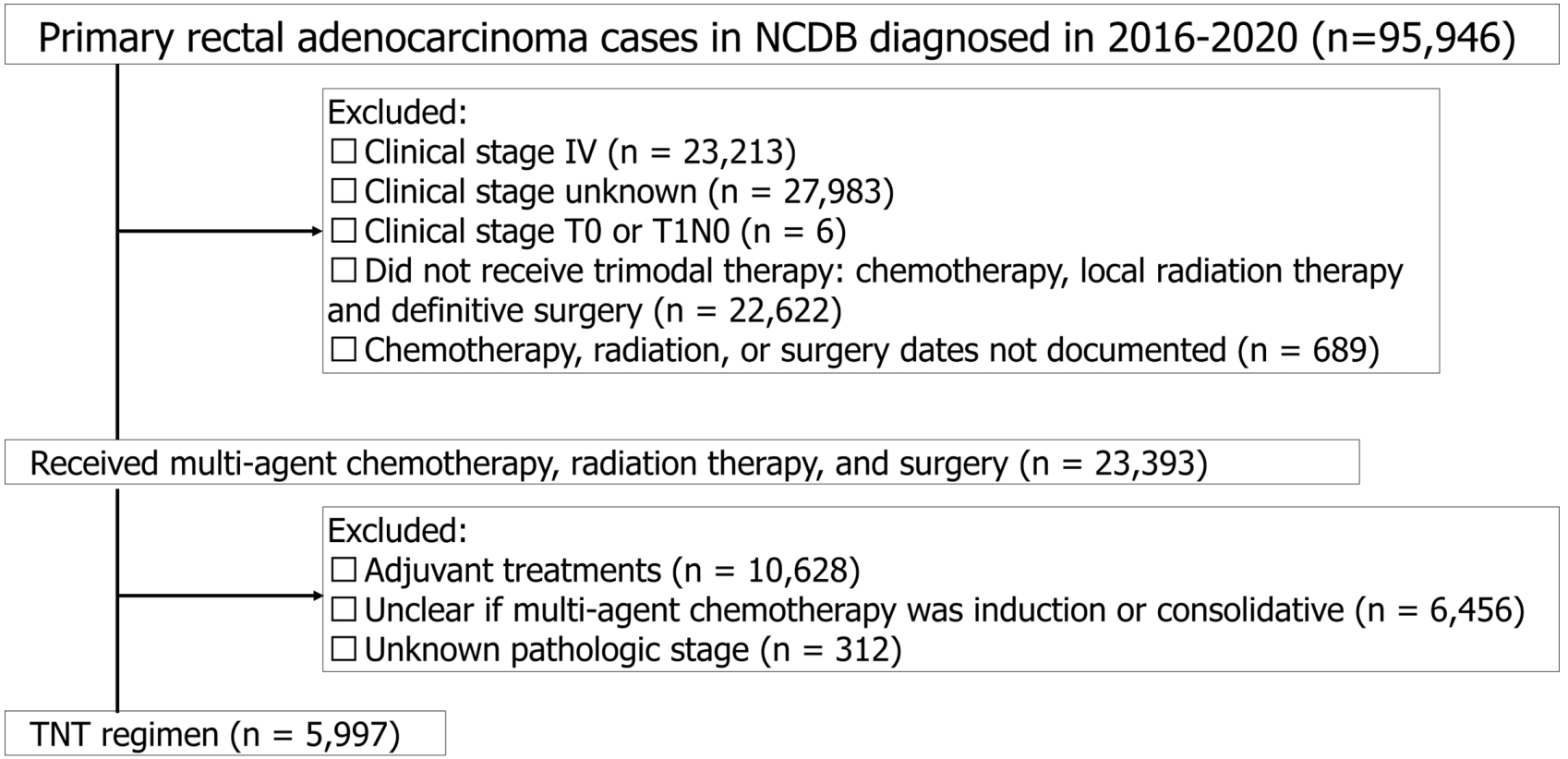
Objective

- To evaluate the relationship between rest period (end of radiation to surgery) and pathologic complete response (pCR) after TNT, using data from the National Cancer Database (NCDB).

National Cancer Database [Internet]. American College of Surgeons. Available from: https://www.facs.org/quality-programs/cancer/ncdb

Methods

- Data source: National Cancer Database (NCDB)
- Inclusion/Exclusion Criteria:



National Cancer Database [Internet]. American College of Surgeons. Available from: https://www.facs.org/quality-programs/cancer/ncdb

Characteristics of patients

	Overall frequency (N=5,997)	No pCR (n=4,888)	pCR (n=1,109)	p-value
Mean age in years (SD)	56.5 (11.4)	56.6 (11.5)	56.3 (11.2)	0.483
Sex				
Male	3,736 (62.3%)	3,220 (86.2%)	516 (13.8%)	0.689
Female	2,261 (37.7%)	1,957 (86.6%)	304 (13.5%)	
Race/Ethnicity				
Non-Hispanic White	4,529 (75.5%)	3,682 (81.3%)	847 (18.7%)	0.871
Hispanic/Latinx	625 (10.4%)	516 (82.6%)	79 (17.4%)	
Non-Hispanic Black	454 (7.6%)	375 (82.6%)	109 (17.4%)	
Non-Hispanic Asian/Pacific Islander	286 (4.8%)	230 (80.4%)	56 (19.6%)	
Other/unknown	103 (1.7%)	85 (82.5%)	18 (17.5%)	
Clinical Stage				
Stage I (T2N0M0)	63 (1.1%)	48 (76.2%)	15 (23.8%)	0.547
Stage II	1,027 (17.1%)	839 (81.7%)	188 (18.3%)	
Stage III	4,907 (81.8%)	4,001 (81.5%)	906 (18.5%)	

National Cancer Database [Internet]. American College of Surgeons. Available from: https://www.facs.org/quality-programs/cancer/ncdb

Characteristics of patients, continued

	No pCR (n=4,888)	pCR (n=1,109)	p-value
Year of Diagnosis			
2016	338 (85.4%)	58 (14.7%)	
2017	439 (84.8%)	79 (15.3%)	0.018
2018	1,088 (81.3%)	251 (18.8%)	
2019	1,552 (81.8%)	345 (18.2%)	
2020	1,471 (79.6%)	376 (20.4%)	
Radiation dosage			
25 Gy in 5 fractions	427 (79.4%)	111 (20.6%)	0.216
45-50 Gy in 25-28 fractions	3,740 (81.4%)	857 (18.6%)	
Nonstandard dose	504 (83.3%)	101 (16.7%)	
Unknown	217 (84.4%)	40 (15.6%)	
TNT regimen			
I-chemotherapy + L-XRT	3,389 (81.0%)	795 (19.0%)	0.107
L-XRT + C-chemotherapy	351 (85.0%)	62 (15.0%)	
S-XRT + C-chemotherapy	225 (77.9%)	64 (22.2%)	
I-chemotherapy + S-XRT	202 (81.1%)	47 (18.9%)	

National Cancer Database [Internet]. American College of Surgeons. Available from: https://www.facs.org/quality-programs/cancer/ncdb

Relation of rest period with pCR

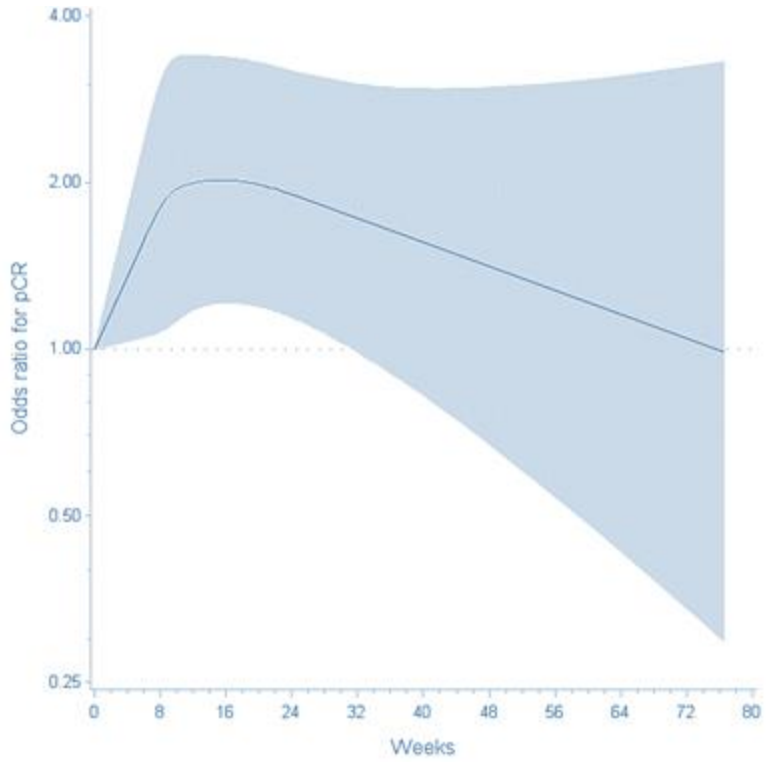


Figure 1. Reference point: 0 weeks. Rest periods of 8.7-24.1 weeks were significantly associated with elevated odds of pCR with the highest odds estimated at 14.6-14.8 weeks [OR 2.86 (95% CI: 1.20 - 6.83)] when compared to surgery <1 week of completing radiation.

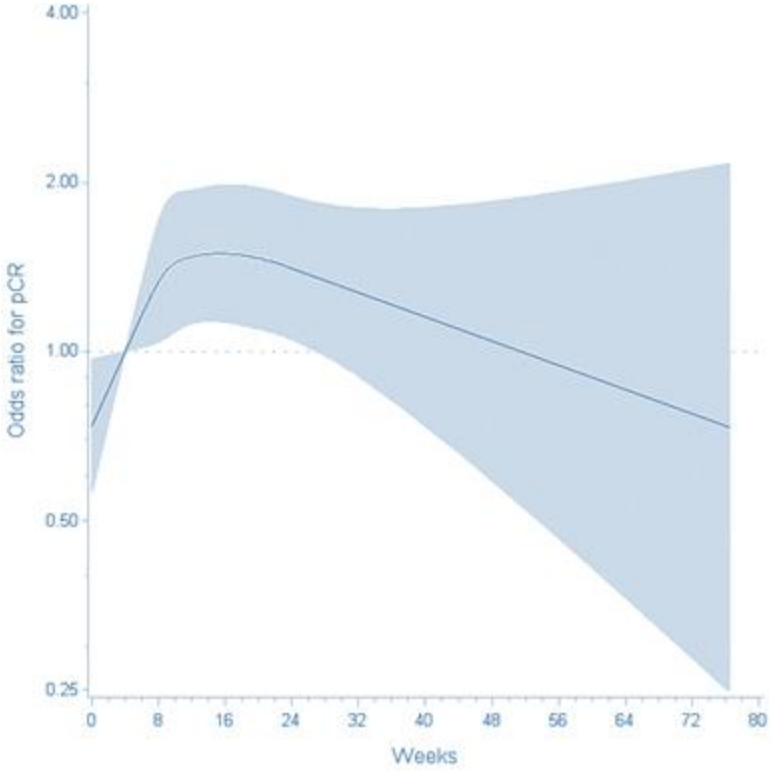


Figure 2. Reference point: 4 weeks. Rest periods of 4.1-26.9 weeks were significantly associated with elevated odds of pCR with the highest odds estimated at 14.7-15.9 weeks [OR 1.49 (95% CI: 1.13-1.97)] when compared to surgery at 4 weeks post-radiation completion.

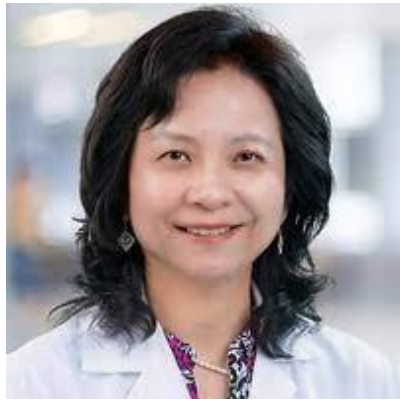
National Cancer Database [Internet]. American College of Surgeons. Available from: https://www.facs.org/quality-programs/cancer/ncdb

Conclusion

- pCR rates are increasing over time
- The relationship between rest period and pCR is non-linear when adjusting for radiation dosage and TNT regimen.
- The odds of pCR peaked around 14.6-14.8 weeks when compared to <1 week and 14.7-15.9 weeks when compared to 4 weeks, independent of radiation dosage and TNT regimen.
- Further prospective investigations are needed to understand the important ways that rest period influence pCR among patients with rectal cancer.

National Cancer Database [Internet]. American College of Surgeons. Available from: https://www.facs.org/quality-programs/cancer/ncdb

Thank you



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