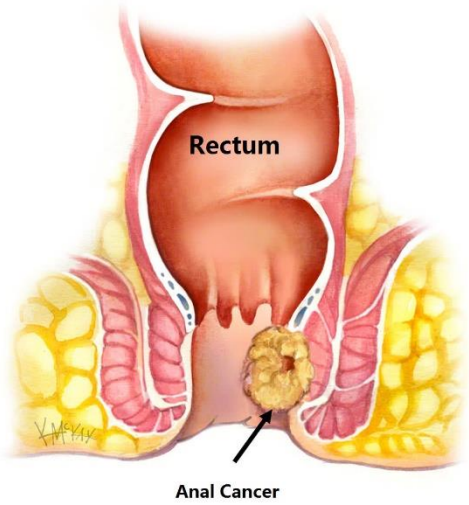
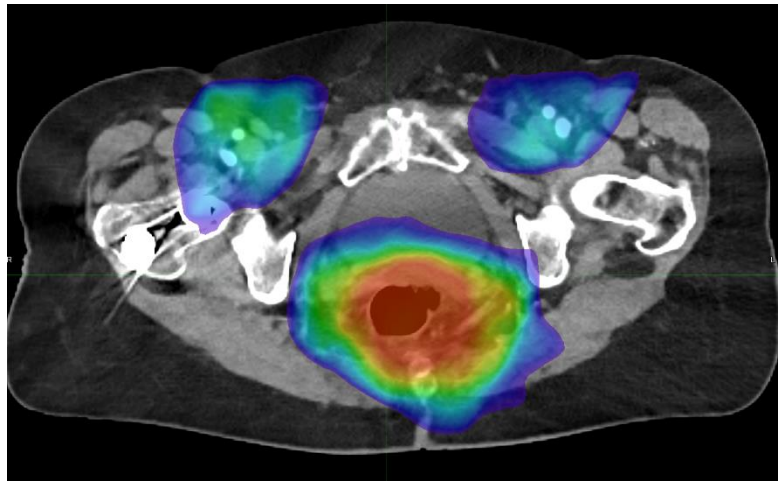
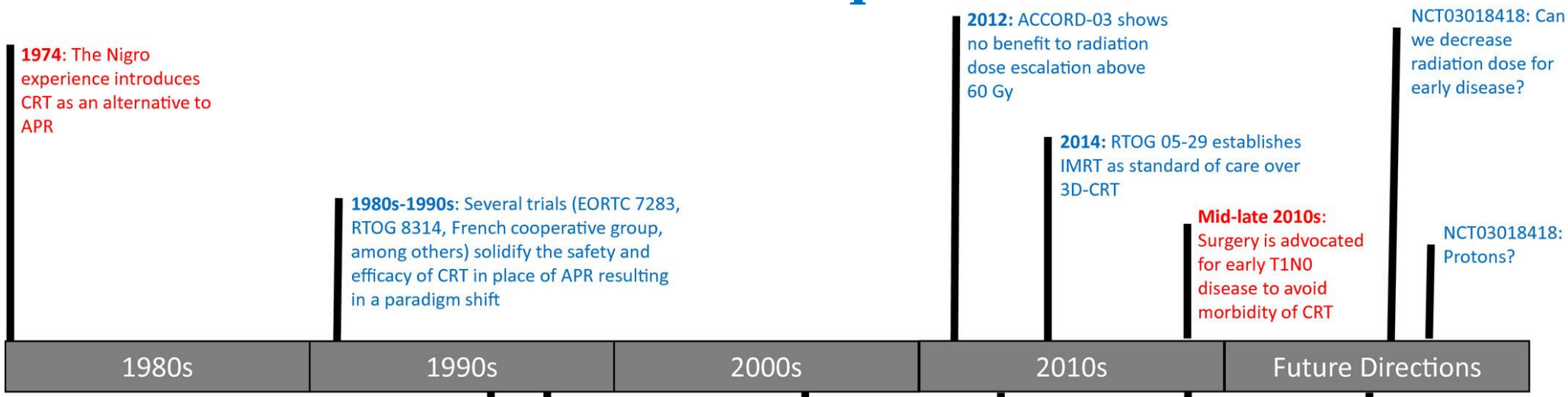
Traitement des petites tumeurs du canal anal



Journée oncologie digestive – St Brieuc
17/11/2023
Aurélien BRIENS, CCA Radiothérapie



Carcinomes épidermoïdes de l'anus
Historique




Norman D. Nigro

Tchelebi et al., CA Cancer, 2021

Recommandations de prise en charge des cancers du canal anal

JNCCN National Comprehensive Cancer Network

OFFICIAL JOURNAL OF THE NATIONAL COMPREHENSIVE CANCER NETWORK

CLINICAL STAGE	PRIMARY TREATMENT[f]	
Locoregional disease[e] →	Mitomycin/5-FU[g] + RT[h] or Mitomycin/capecitabine[g] + RT[h] or 5-FU/cisplatin[g] + RT[h] (category 2B)	→ See Follow-up Therapy and Surveillance (ANAL-3)

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ANNALS OF ONCOLOGY driving innovation in oncology — ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Stage II-III anal margin
Stage I-III anal canal

↓

Definitive CRT[a]:
RT dose of >50 Gy
(optimal dose unknown) [III, B]
5-FU + MMC [I, A]
Capecitabine replacing 5-FU [III, B]

T2-T4

N0-N3

REFERENCES

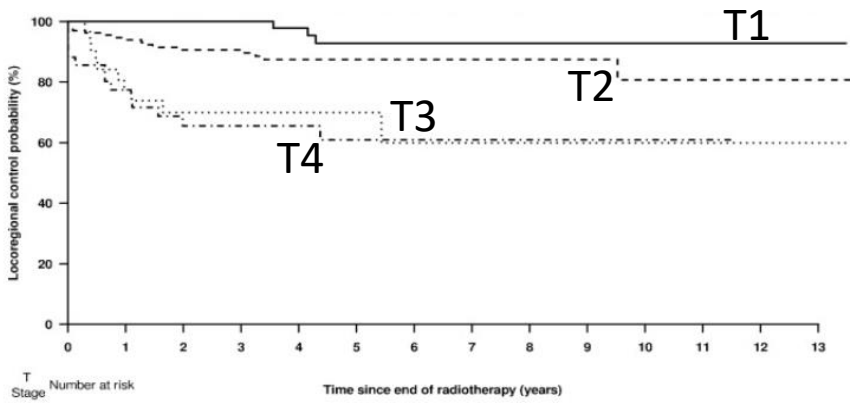
- Association chimio-radiothérapie concomitante exclusive 5FU-Mitomycine C

Benson *et al.,* JNCCN, 2018 ; Rao *et al.,* Ann Oncol, 2021 ; Moureau-Zabotto *et al.*, Dig Liver Dis., 2017

Problématique des stades précoces

- Peu de patients inclus dans les essais de phase III

Source (Study)	No. of Patients Included	Purpose	Inclusion Criteria
Nigro et al,[3] 1974	3	Preliminary report of preoperative use of concurrent chemoradiotherapy	T2 anal canal tumor
Cummings et al,[9] 1980	6	Case report of chemoradiotherapy as definitive treatment	T2-3N0-X anal canal tumor with extension to margin
Nigro et al,[10] 1983	28	Preoperative chemoradiotherapy followed by surgery to assess treatment response	T2 or greater anal canal tumor
UKCCCR Anal Cancer Trial Working Party,[11] 1996 (UKCCCR ACT I)	585	Chemoradiotherapy vs radiotherapy	Anal cancer (T1N0 tumors suitable for local excision were not randomized)
Bartelink et al,[12] 1997 (EORTC)	110	Chemoradiotherapy vs radiotherapy	T1-2N1-3, T3-4N0-3, age <76 y, ECOG stage 0-1
Flam et al,[13] 1996 (RTOG 87-04 [phase 3])	291	Chemoradiotherapy with fluorouracil vs chemoradiotherapy with fluorouracil and mitomycin C	Anal canal cancer, Karnofsky Performance Status score ≥60, nodal status (N0 vs N1), tumor size (<5 vs ≥5 cm) (15% with T1NX disease)
Gunderson et al,[14] 2012 (RTOG 98-11 [phase 3])	644	Chemoradiotherapy vs induction chemotherapy and chemoradiotherapy	Anal canal cancer, age ≥18 y, Karnofsky Performance Status score ≥60, T2-4 with any N
James et al,[15] 2013 (ACT II [phase 3])	940	Chemoradiotherapy with fluorouracil and mitomycin C vs chemoradiotherapy with fluorouracil and cisplatin	Anal cancer (9.7% with T1NX disease)



- Pronostic des tumeurs T1 et T2 N0 favorable

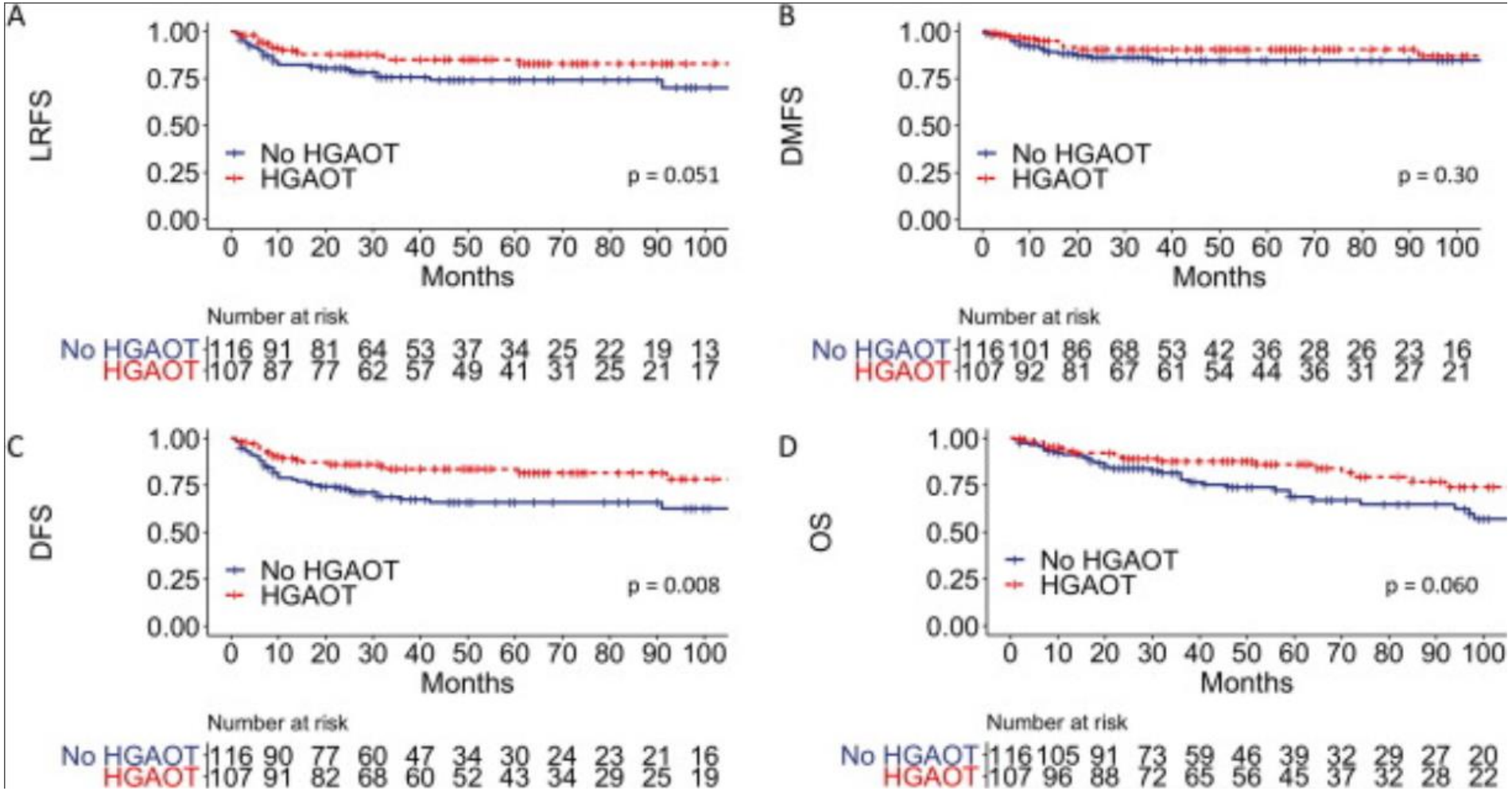
- Toxicités de la radio-chimiothérapie

Toxicity	CTCAE Grade	n (%)
Dermatitis	0	6 (3)
	1	31 (14)
	2	95 (43)
	3	91 (40)
	4	0 (0)
Diarrhea	0	81 (36)
	1	77 (34)
	2	46 (21)
	3	18 (8)
	4	1 (1)
Proctitis	0	103 (46)
	1	66 (30)
	2	49 (22)
	3	5 (2)
	4	0 (0)
Cystitis	0	151 (68)
	1	53 (24)
	2	17 (7)
	3	2 (1)
	4	0 (0)
Total toxicity	≥3	117 (52)

Chai et al., JAMA Surgery, 2018

Tomasczewski et al., IJROBP, 2012.

Martin et al., Radiother and Oncology, 2020

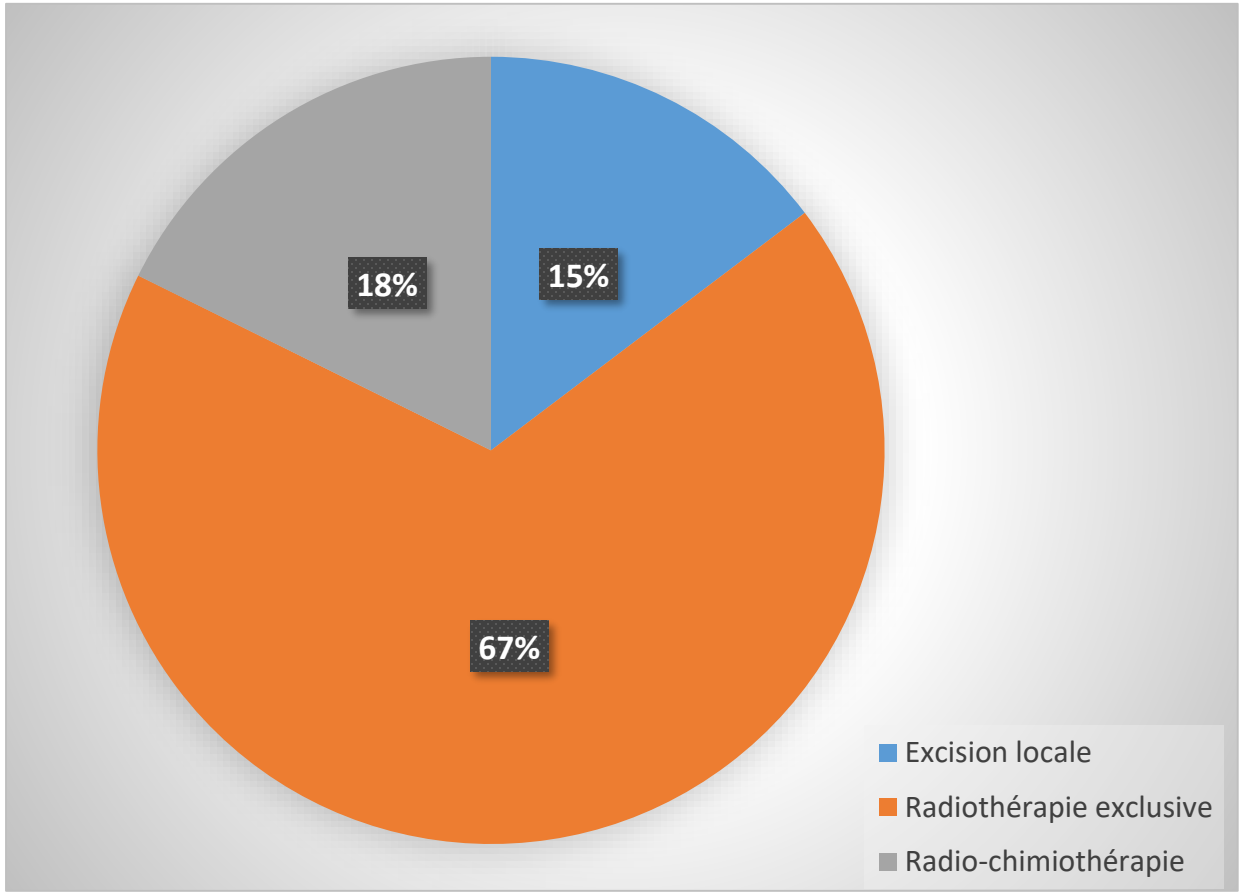


- La toxicité sévère est associée à un meilleur pronostic oncologique.

Martin et al., Radiother and Oncol, 2020

Quels traitements en France pour les tumeurs de l'anus de stade précoce ?

- Cohorte FFCD ANABASE
- 2015-2020
- 1135 patients SCCA
  - 100 T1N0



Adapté de Bacci et al., Digestive and Liver Disease, 2021

Recommandations pour les stades précoces

JNCCN National Comprehensive Cancer Network
OFFICIAL JOURNAL OF THE NATIONAL COMPREHENSIVE CANCER NETWORK

CLINICAL STAGE	PRIMARY TREATMENT[f]	
Locoregional disease[e]	Mitomycin/5-FU[g] + RT[h] or Mitomycin/capecitabine[g] + RT[h] or 5-FU/cisplatin[g] + RT[h] (category 2B)	See Follow-up Therapy and Surveillance (ANAL-3)

Recommendations for the primary treatment of perianal cancer and anal canal cancer are very similar and **include chemoRT in most cases**. The exception is **small, well or moderately differentiated perianal lesions and superficially invasive lesions**, which can be treated with margin-negative **local excision alone.**

ANNALS OF ONCOLOGY — ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Relatively few patients with stage I disease were included in the CRT trials and so application of overall data to T1 tumours is limited. However, for small tumours (T1), some investigators have used external beam RT alone followed by a small volume boost. In contrast, early investigators[34,41] reported that CRT with the addition of MMC to 5-FU demonstrated excellent local control in small tumours (<4 cm).

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6.5.3. Stades usT1 N0 (cf. 6.7.1. Arbre décisionnel 1)

- **Pour les carcinomes épidermoïdes du canal anal**
  - **la radiothérapie exclusive** constitue le traitement de première intention permettant d'obtenir la conservation du sphincter et un taux élevé de contrôle loco-régional ***(accord d'expert)***

6.5.4. Stades T2N0 ou N1 / T2N3 /T3 /T4 (cf. 6.7.2. Arbre décisionnel 2)

- **Association chimio-radiothérapie avec 5FU–Mitomycine C concomitante**

OPTIONS

- **Radiothérapie exclusive :** option pour les tumeurs "T2 N0 faible" c'est à dire de moins de 3 cm ***(accord d'experts)***, même si pour ces lésions, l'apport de la chimiothérapie reste intéressant (Zilli 2012).

Benson *et al.,* JNCCN, 2018 ; Rao *et al.,* Ann Oncol, 2021 ; Moureau-Zabotto *et al.*, Dig Liver Dis., 2017

Radiothérapie exclusive des stades précoces

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

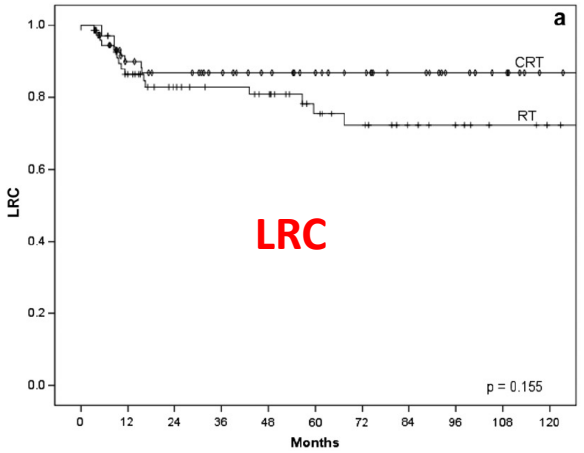
Anal cancer

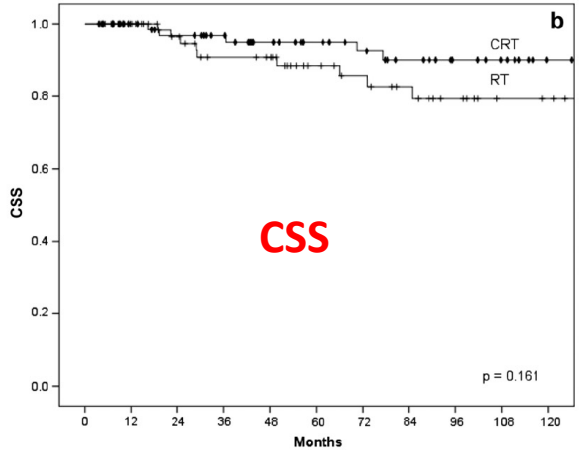
Node-negative T1–T2 anal cancer: Radiotherapy alone or concomitant chemoradiotherapy?

Thomas Zilli [a,*], Ulrike Schick [a], Mahmut Ozsahin [a,c], Pascal Gervaz [b], Arnaud D. Roth [b], Abdelkarim S. Allal [a,d]

Cox regression analysis for loco-regional control, $n = 146$.

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Age, y[a]	0.99 (0.95–1.02)	0.595	0.98 (0.95–1.02)	0.330
Gender[b]				
Female *vs.* male	1.36 (0.51–3.64)	0.540	1.31 (0.48–3.51)	0.599
AJCC clinical T-stage[b]				
T1 *vs.* T2	0.35 (0.08–1.49)	0.155	0.27 (0.06–1.23)	0.091
OTT, days[a]	1.01 (0.99–1.02)	0.302	1.00 (0.99–1.01)	0.746
Treatment strategy[b]				
RT *vs.* CRT	1.80 (0.79–4.13)	0.161	2.23 (0.95–5.23)	0.065





	RT	RTCT	p-value	Nb patients
Global	75,5 %	86,8 %	p=0,155	146
0-2 cm	88,9 %	100 %	p=0,216	29
2-3 cm	70 %	79,4 %	p=0,715	53
3-4 cm	70,1 %	79,5 %	p=0,715	36
4-5 cm	69,3 %	85,4 %	p=0,286	24

*"Interestingly, **the prognosis was excellent for tumors ⩽3 cm** in length, presenting a LRC of more than 85% at five years, **independently of the treatment modality**."*

Intérêt de la radiothérapie exclusive des stades précoces

Toxicités		RT exclusive	RTCT
Aiguës	Toutes toxicités	16%	56%
	Interruptions de traitement non planifiée	16%	19%
Tardives	Toutes toxicités	36%	44%
	Colostomies pour complications	4%	19%

- Toxicités acceptables en adoptant un schéma de radiothérapie en split-course.

Adapté de Cummings et al., Cancer, 1984

Etude de registre : 299 patients, SCCA stade 1

- 200 traités par RTCT
- 99 traités par RT exclusive

Entre 1996 et 2011

	Unmatched	
	Odds Ratio (95% CI)	*p*
Early toxicities		
Pain	2.5 (1.1–5.9)	0.04
Proctitis	2.9 (1.5–5.6)	<0.01
Late toxicities		
Bleeding	2.0 (1.2–3.5)	0.01
Proctitis	2.7 (1.5–4.8)	<0.01
Chemotherapy-associated		
Dehydration	3.1 (1.5–6.5)	<0.01
Electrolyte abnormality	2.3 (1.1–4.8)	0.03
Emesis	3.4 (1.8–6.5)	<0.01
Neutropenia	4 (1.6–9.8)	<0.01

Buckstein et al., Disease Colon Rectum, 2019

Home > International Journal of Colorectal Disease > Article

Radiotherapy alone versus chemoradiotherapy for stage I anal squamous cell carcinoma: a systematic review and meta-analysis

Review | Published: 24 January 2021 | 36, 1111–1122 (2021)

Gaurav Talwar, Ryan Daniel, Tyler McKechnie, Oren Levine & Cagla Eskicioglu

International Journal of Colorectal Disease

Aims and scope →

Submit manuscript →

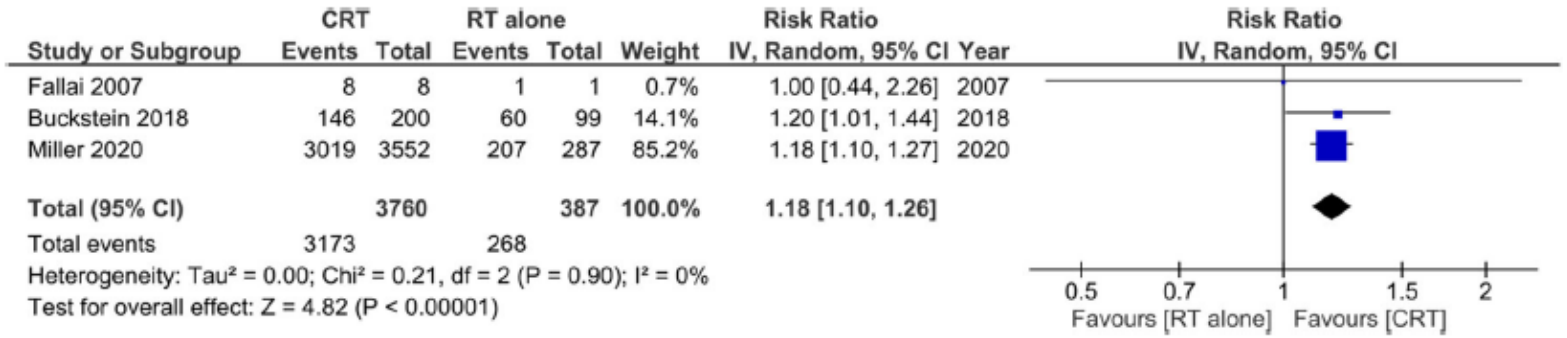


Fig. 2 5-year overall survival. Random-effects meta-analysis comparing treatment with chemoradiotherapy and radiotherapy alone

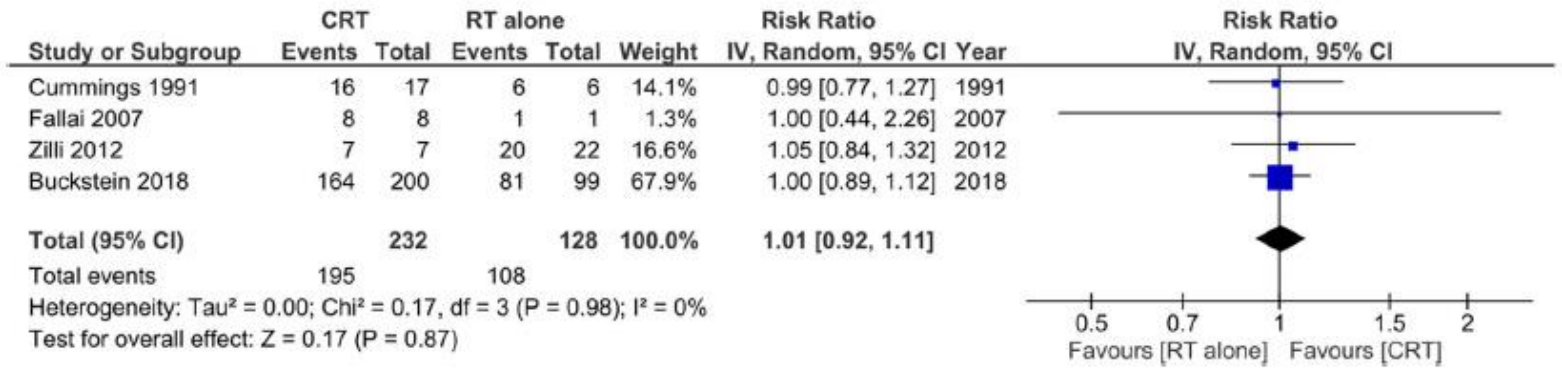


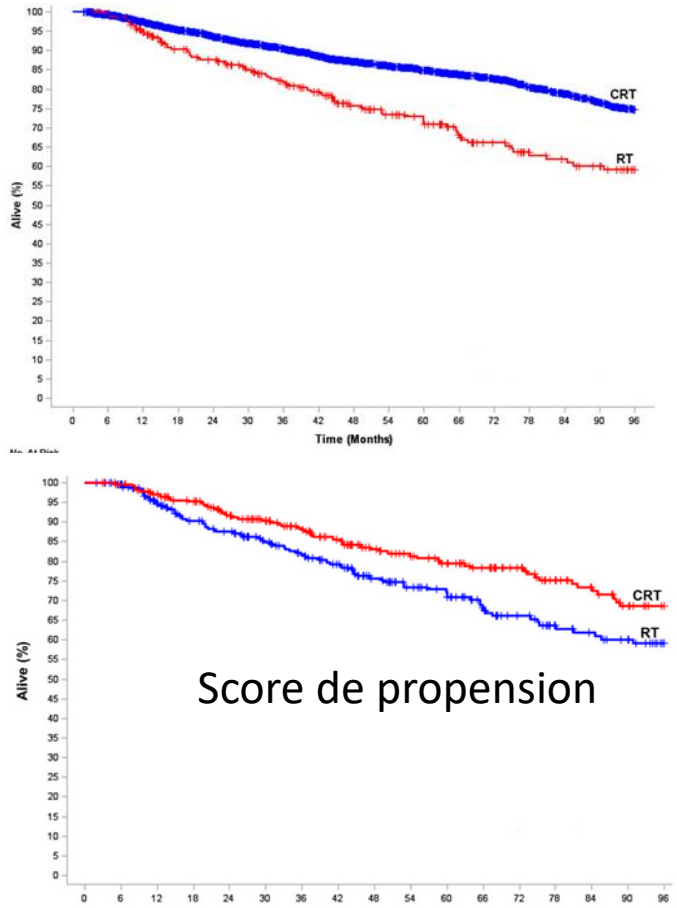
Fig. 3 5-year disease-free survival. Random-effects meta-analysis comparing treatment with chemoradiotherapy and radiotherapy alone

RT exclusive des stades précoces : biais possibles

Etude de registre : SCCA T1 N0 traités par :

- RTCT : 3552 patients
- RT exclusive : 287 patients

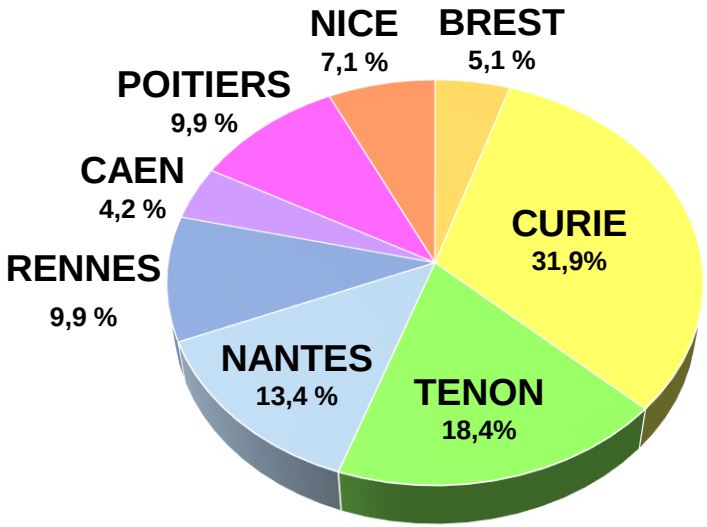
RT Alone vs. CRT	Univariate Analysis			Multivariate Analysis		
Variable	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Age (years)						
<50	1.62	1.13–2.32	0.009	1.42	0.98–2.05	0.064
50–59	Ref	Ref	Ref	Ref	Ref	Ref
60–69	1.13	0.80–1.60	0.498	1.15	0.81–1.63	0.437
≥70	2.38	1.72–3.30	<0.001	2.45	1.76–3.39	<0.001
Female vs. male	0.70	0.54–0.90	0.005	0.76	0.58–0.98	0.036
Charlson–Deyo score						
0	Ref	Ref	Ref	Ref	Ref	Ref
1	0.94	0.64–1.40	0.769	0.86	0.58–1.29	0.476
2–3	1.50	0.97–2.32	0.068	1.26	0.80–1.99	0.315
White vs. non–white	0.70	0.48–1.01	0.055	0.72	0.49–1.05	0.089
Academic vs. non–academic	1.10	0.85–1.44	0.460	——	——	——
Uninsured vs. insured	1.11	0.55–2.21	0.775	——	——	——
Median income (<$46 K/yr vs. ≥$46 K/yr)	1.21	0.94–1.55	0.146	1.15	0.89–1.49	0.276
Tumor Size						
≤1 cm	Ref	Ref	Ref	Ref	Ref	Ref
1–2 cm	0.71	0.53–0.96	0.024	0.69	0.51–0.93	0.014
Unknown	1.07	0.77–1.48	0.683	1.01	0.72–1.40	0.975
Distance (per mile)	1.00	1.00–1.00	0.544	——	——	——



Score de propension

Miller et al., Cancers, 2020.

141 PATIENTS, SCCA stade précoce traités par RT exclusive



Age médian : 63 ans
75 % femmes
Bon état général : 96 % PS 0-1
HIV positif : 11,5 %
HPV positif : 22 % (inconnu 64 %)

Radiothérapie

Dose totale : 62 Gy

53 jours

1e phase : 45 Gy / 25 fractions de 1,8 Gy

5 semaines

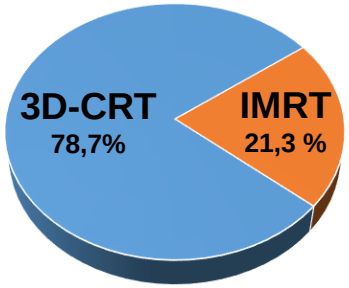
- Irradiation pelvienne : 82,3 %
- Irradiation inguinale : 50,4 %

Gap : 80,9 %

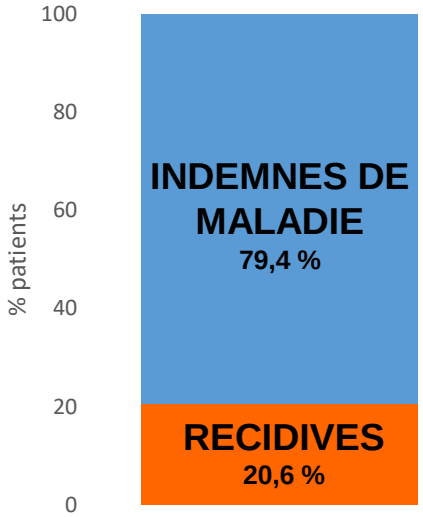
3 semaines

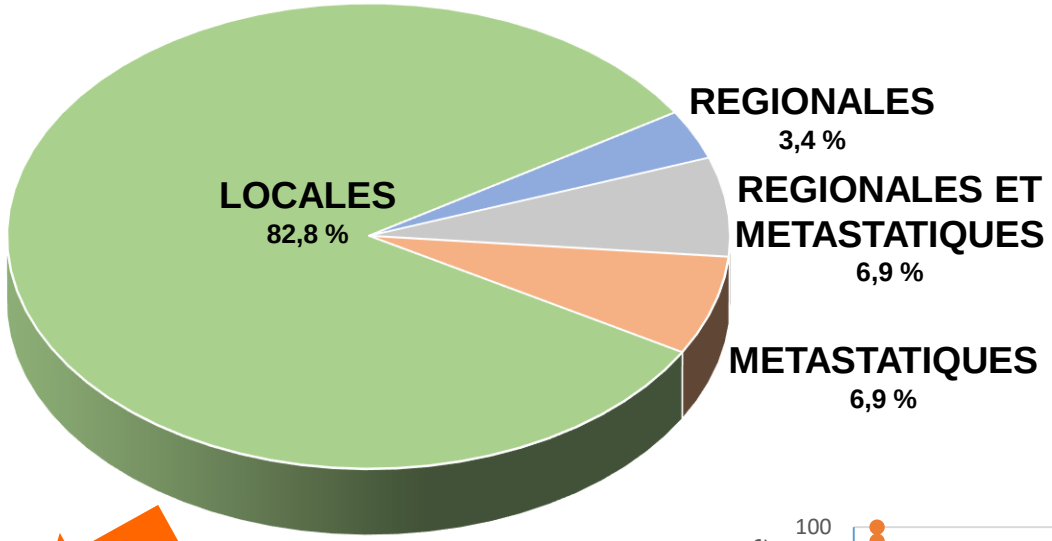
Boost : 18 Gy / 10 fractions

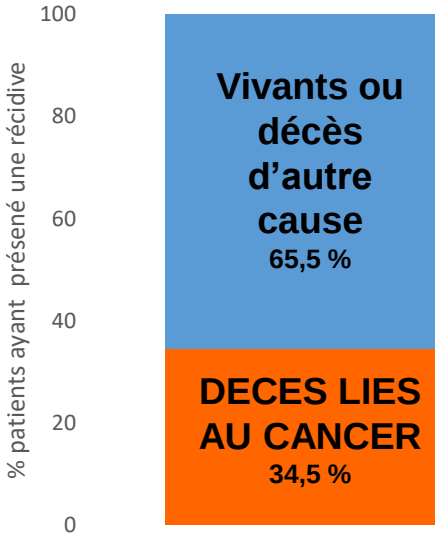
- RT externe : 78,1 %
- Curiethérapie 21,9 %

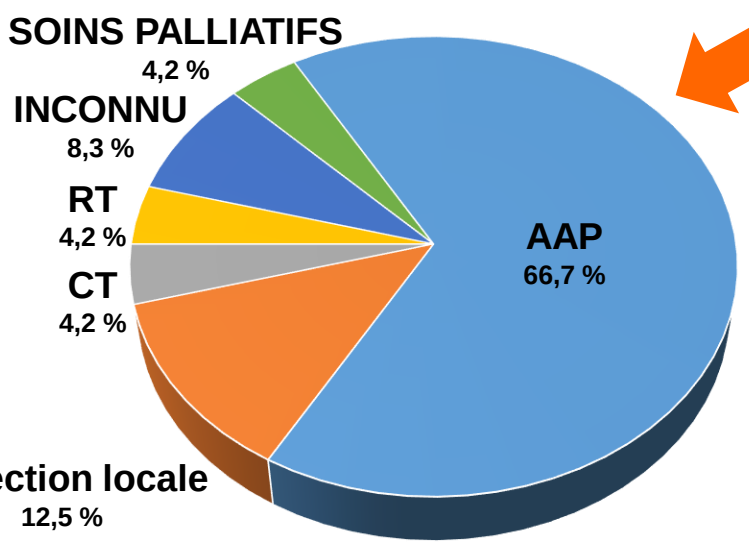


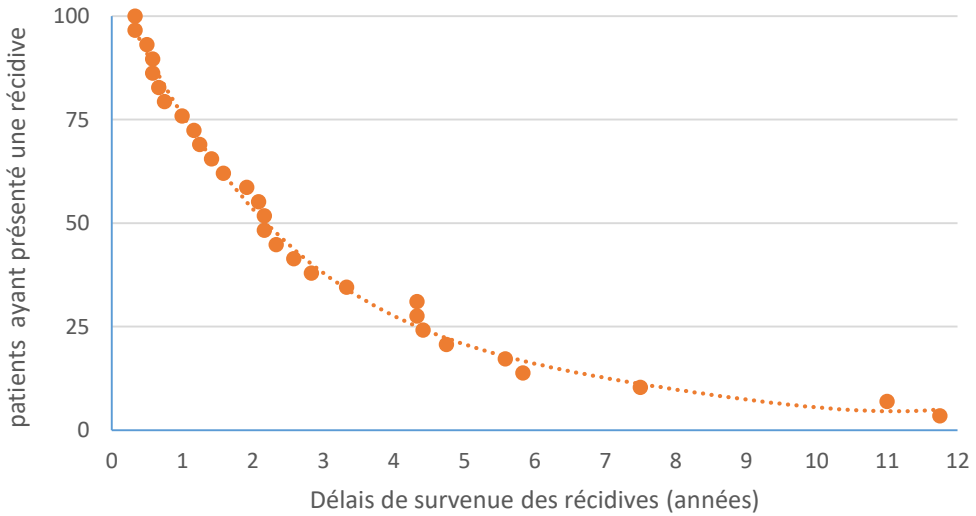
Suivi médian de 56 mois.





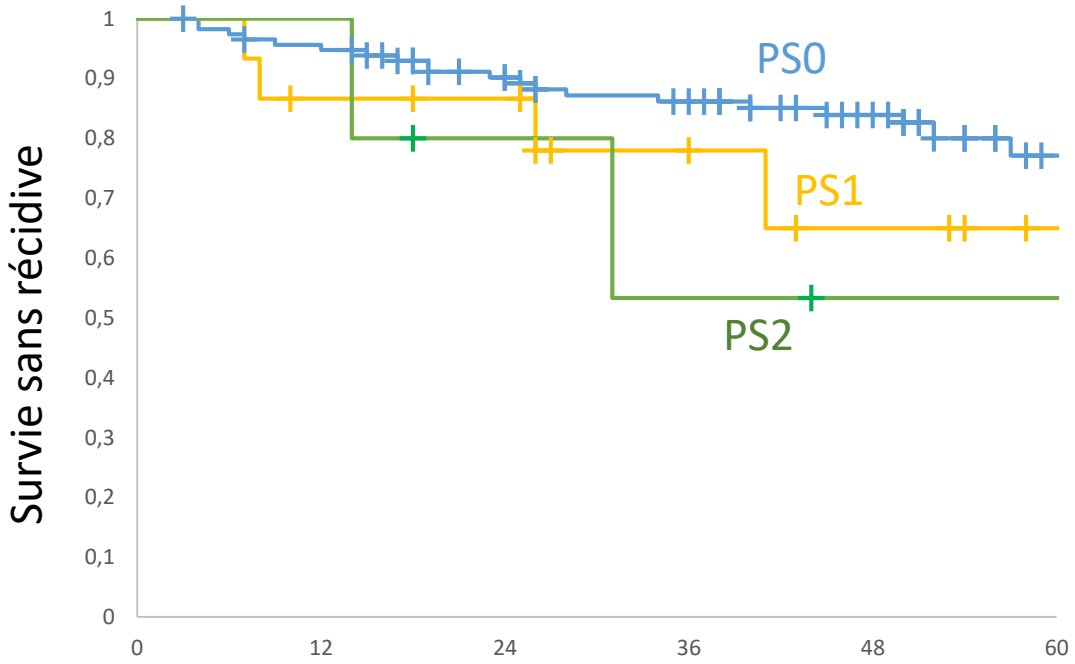






Facteurs prédictifs de survie sans récidive : l'état général

	Univarié		Multivarié	
	HR	p-value	HR	p-value
Sexe	0.72 (0.36-1.44)	.353		
Age	1.01 (0.98-1.03)	.614		
Performance status	**2.05 (1.20-3.50)**	**.009**	**3.87 (1.13-13.24)**	**.031**
Histologie, bien différencie	1.06 (0.47-2.41)	.888		
VIH	1.73 (0.75-4.00)	.195		
Bilan locorégional correct	**0.44 (0.21-0.93)**	**.031**	1.70 (0.82-3.54)	.465
Bilan à distance correct	1.00 (0.49-2.00)	.995		
Taille tumorale	1.01 (0.60-1.68)	.980		
Irradiation pelvienne	0.63 (0.29-1.39)	.255		
Irradiation inguinale	1.59 (0.83-3.05)	.164		
Boost en curiethérapie	0.53 (0.22-1.27)	.155		
Gap	1.01 (0.98-1.03)	.519		
Dose totale	0.96 (0.91-1.02)	.182		
Technique de radiothérapie, IMRT	1.15 (0.47-2.82)	.755		
Etalement, > 70 jours	**1.94 (1.00-3.77)**	**.051**	1.70 (0.82-3.54)	.157



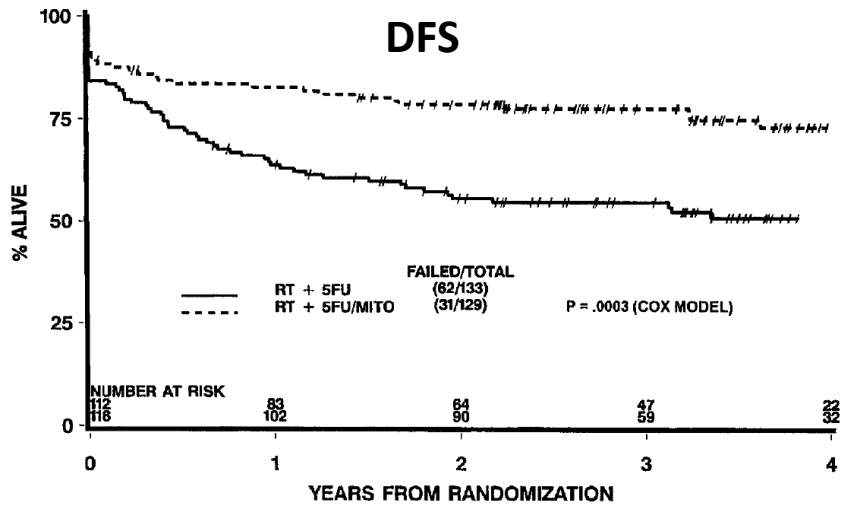
- Peu d'études, rétrospectives, petits effectifs.
- La plupart des études en faveur d'un bénéfice de la radiochimiothérapie sur la radiothérapie exclusive dans cette population en contrôle local et survie globale.
- Bénéfice plus controversé en survie sans récidive.
- Attention aux biais dans l'interprétation des résultats : patients à qui on propose la radiothérapie exclusive plus âgés, possiblement en moins bon état général.
- Or l'altération de l'état général semble associée à une moins bonne survie sans récidive après radiothérapie exclusive
- Toxicités de la radio-chimiothérapie restent très importantes.
- La RT exclusive dans cette population représente une option thérapeutique avec de bons résultats oncologiques avec une moindre toxicité chez la majorité des patients.

Modalités de la chimiothérapie

RTOG 57-04

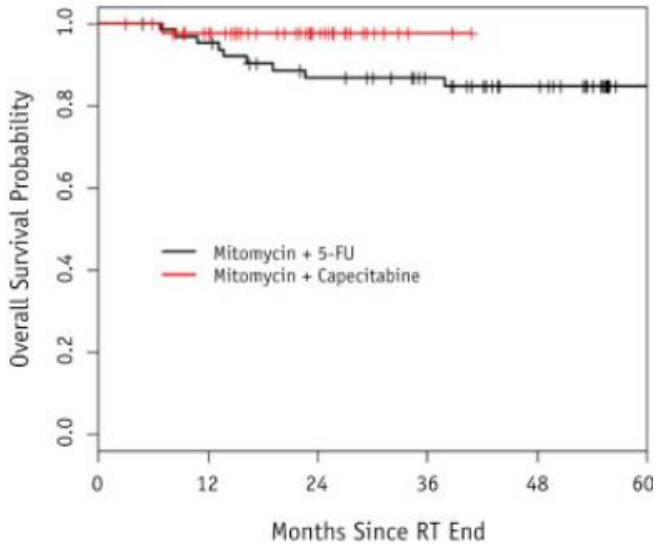
5-FU + MMC > 5-FU

Tumor stage				
T1	22	15	22	15
T2	50	35	61	42
T3	61	42	48	33
T4	12	8	15	10
Nodal stage				
N0	119	82	121	83
N1	25	17	25	17
NX	1	1	0	0



Flam et al., JCO, 1996.

5-FU/Capecitabine



Variable	Mitomycin + 5-FU (n=63)	Mitomycin + capecitabine (n=44)	*P* value
Hematologic toxicity			
Grade 3+			
Neutropenia	33 (52%)	9 (20%)	.001
Leukopenia	34 (54%)	14 (32%)	.03
Thrombocytopenia	10 (16%)	4 (9%)	.39
Anemia	5 (8%)	3 (7%)	.40
Nonhematologic toxicity			
Grade 3			
Diarrhea	0 (0%)	1 (2%)	.41
Dermatitis	8 (13%)	1 (2%)	.08
Oral mucositis	1 (2%)	0 (0%)	1.00
Treatment break	26 (41%)	7 (16%)	.006
Median treatment duration (days)	39 (range, 32-52)	37 (range, 32-44)	<.001

Goodman et al., IJROBP, 2017.

Modalités de la radiothérapie : IMRT

RTOG 0529

- Essai de phase II
- 52 patients
- T2-T4, N0-N3, M0
- Tous traités par IMRT

Adverse events	0529 (n=52)	98-11 (Arm 1 †) (n=325)	*P* value (1-sided proportions test §)
Grade 2+			
GI/GU ‡	40 (77%)	249 (77%)	.50
Derm	39 (75%)	271 (83%)	.10
GI	38 (73%)	237 (73%)	.50
GU	8 (15%)	66 (20%)	.18
Heme	38 (73%)	275 (85%)	.032
Overall	49 (94%)	318 (98%)	.12
Grade 3+			
GI/GU	11 (21%)	120 (37%)	.0052
Derm	12 (23%)	159 (49%)	<.0001
GI	11 (21%)	117 (36%)	.0082
GU	1 (2%)	11 (3%)	.32
Heme	30 (58%)	201 (62%)	.29
Overall	43 (83%)	283 (87%)	.23

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The consensus of the panel is that IMRT is preferred over 3D conformal RT in the treatment of anal carcinoma.[191] IMRT requires expertise and careful target design to avoid reduction in local control by marginal miss.[114]

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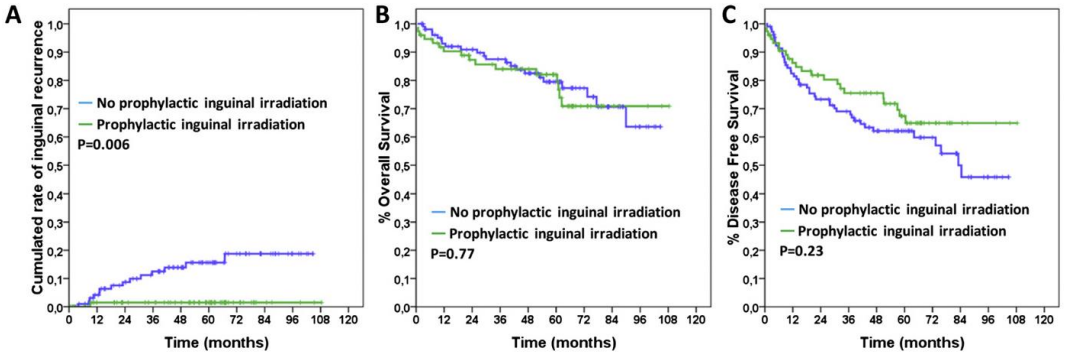
IMRT or volumetric modulated arc therapy (VMAT) is currently recommended for the treatment of anal cancer, setting strict RT dose constraints to normal organs [III, B].

Kachnic et al., IJROBP, 2013.

Modalités de la radiothérapie : réduction de volume

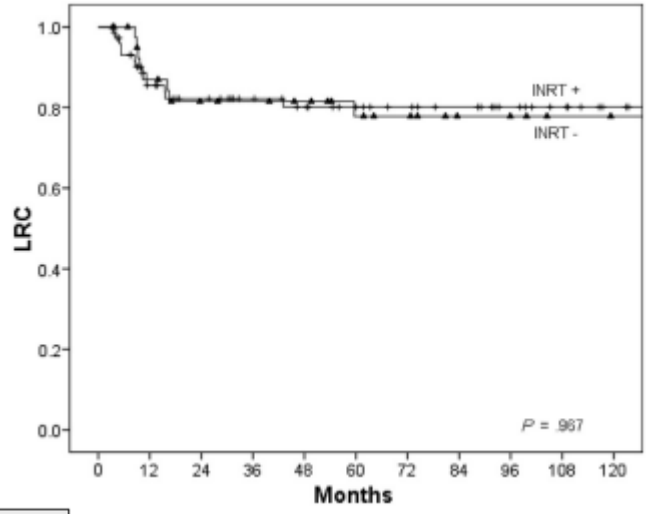
Controverse sur l'intérêt de l'irradiation inguinale dans cette population.



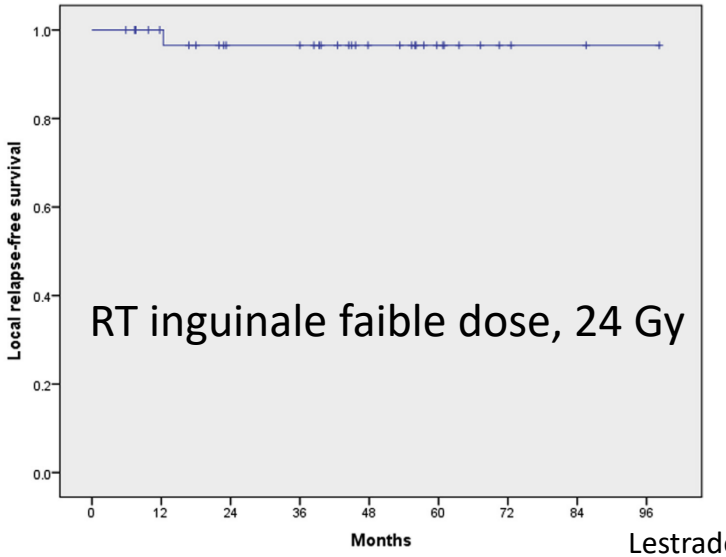
No prophylactic inguinal irradiation group

Factors	Categories	5-year cumulative rate of inguinal recurrence	*p* value
T stage	T1-T2	12%	0.02
	T3-T4	30%	

Ortholan et al., IJROBP, 2012



Zilli et al., IJROBP, 2013



RT inguinale faible dose, 24 Gy

Lestrade et al., Clinical Oncology, 2017

Niveaux de preuve très faible pour émettre des recommandations formelles.

Modalités de la radiothérapie : réduction de doses

- Protocole NIGRO initial : 30 Gy / 15 fractions
- Doses < 50 Gy associées à plus d'échecs locorégionaux par rapport à > 54 Gy pour les tumeurs plus avancées.
- 2 essais thérapeutiques en cours

DECREASE EORTC
T1-T2 < 4 cm, N0

- 50,4 Gy en 28 fractions + Mitomycine/5-Fu
- 36 à 41,4 Gy en 20 à 23 fractions + Mitomycine/5-Fu

Phase II
Objectif : survie sans récidive à 2 ans

ACT IV
Cancer Research UK

- 50,4 Gy en 28 fractions + Mitomycine/Capecitabine
- 41,4 Gy en 23 fractions + Mitomycine/Capecitabine

" Overall for PROs, there was a large to moderate deterioration in pain, fatigue, overall bowel function, quality of life, physical, role and social function at the end of CRT which resolved to baseline by either 6 weeks or 6 months ***in both arms.*** *"*

Toxicity and maximum grade experienced	Standard dose IMRT (50.4 Gy 28F) (n=55)	Reduced dose IMRT (41.4 Gy 23F) (n=105)	Total (n=160)
Dermatitis radiation			
0	20 (36.4%)	41 (39.0%)	61 (38.1%)
2	28 (50.9%)	54 (51.4%)	82 (51.3%)
3	7 (12.7%)	10 (9.5%)	17 (10.6%)
Diarrhoea			
0	41 (74.5%)	73 (69.5%)	114 (71.3%)
2	10 (18.2%)	23 (21.9%)	33 (20.6%)
3	3 (5.5%)	9 (8.6%)	12 (7.5%)
4	1 (1.8%)	0 (0.0%)	1 (0.6%)
Dysuria			
0	52 (94.5%)	103 (98.1%)	155 (96.9%)
2	3 (5.5%)	2 (1.9%)	5 (3.1%)
Fatigue			
0	41 (74.5%)	80 (76.2%)	121 (75.6%)
2	11 (20.0%)	23 (21.9%)	34 (21.3%)
3	3 (5.5%)	2 (1.9%)	5 (3.1%)
Neutropenia			
0	50 (90.9%)	92 (87.6%)	142 (88.8%)
2	3 (5.5%)	7 (6.7%)	10 (6.3%)
3	1 (1.8%)	6 (5.7%)	7 (4.4%)

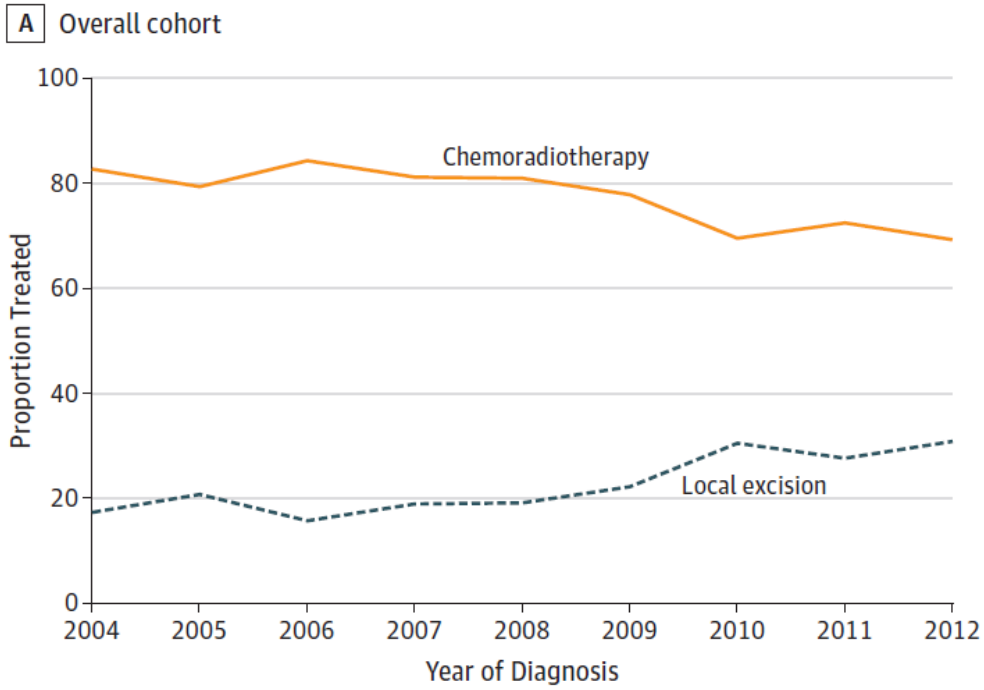
Gilbert et al., poster ESTRO, 2023

JAMA Surgery | Original Investigation | ASSOCIATION OF VA SURGEONS

Management of Stage I Squamous Cell Carcinoma of the Anal Canal

Christy Y. Chai, MD; Hop Tran Cao, MD; Samir Awad, MD, MPH; Nader N. Massarweh, MD, MPH

Etude rétrospective de registre
2243 patients T1N0 (NCDB)
Excision locale 503 (22%)
Radio-chimiothérapie : 1740 (78%)



Chai et al, JAMA Surgery, 2018

Author	Year	Single center	Design	NOS selection	NOS comparability	NOS outcome	*N* patients
Cortese [11]	1932–1975	Yes	Retrospective	***	*	***	8
Dillard [12]	1940–1957	No	Retrospective	***	*	***	14
Merlini [13]	1942–1983	Yes	Retrospective	***	*	***	14
Jensen [14]	1943–1974	–	Retrospective	***	*	***	AC: 21 AM: 32
Stearns [15]	1944–63	Yes	Retrospective	***	*	***	30
Golden [16]	1945–1969	Yes	Retrospective	***	*	***	2
Pintor [17]	1948–84	Yes	Retrospective	***	*	***	AC: 8 AM: 41
Boman [18]	1950–1976	Yes	Retrospective	***	*	***	12
Greenall [19]	1950–1978	Yes	Retrospective	***	*	***	31
Al-Jurf [20]	1951–1971	Yes	Retrospective	***	*	***	10
Bohe [21]	1958–77	Yes	Retrospective	***	*	***	5
Christiansen [22]	1962–1971	Yes	Retrospective	***	*	***	4
Cuthbertson [23]	1962–1977	Yes	Retrospective	***	*	**	5
Hardy [24]	1969	No	Retrospective	***	*	**	6
Lorenz [25]	1980–1988	Yes	Retrospective	**	*	*	1
Alfa-Walli [26]	1986–2015	Yes	Prospective	***	*	***	15
Chakrabarti [27]	1990–2016	No	Retrospective	***	*	***	13
Deshmukh [28]	1992–2009	No	Retrospective	***	*	***	44
Leon [29]	2000–2007	Yes	Retrospective	***	*	***	52
Suradkar [30]	2004–2013	Yes	Retrospective	***	*	***	382
Chai [31]	2004–2014	No	Retrospective	***	*	***	503
Gao [32]	2004–2015	No	Retrospective	***	*	***	200
Arana [33]	2007–2009	Yes	Retrospective	***	*	***	5

AC: Anal Canal. AM: Anal margin

*"Data on complications following local excision was available in two studies only. **No complications** were reported."*

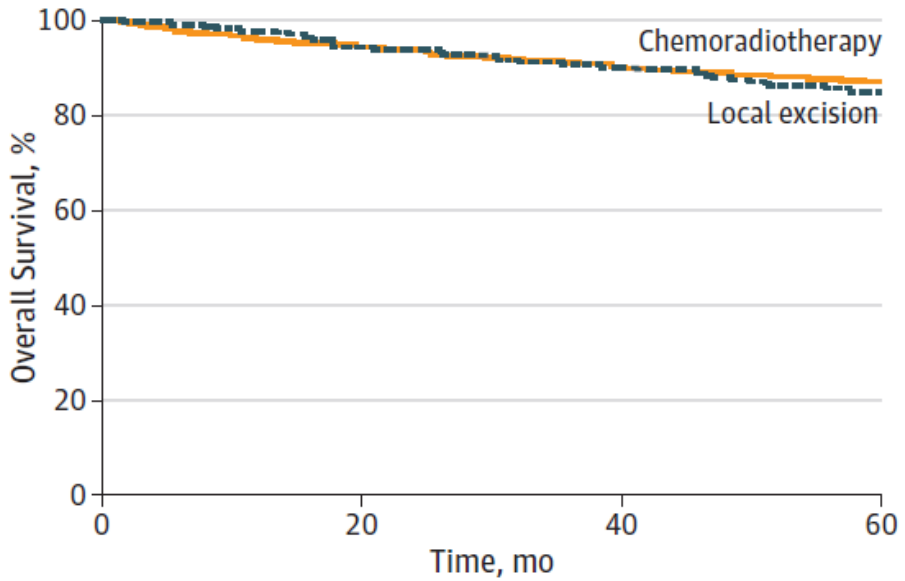
Pedersen et al., Int J Colorectal Disease, 2020

	Mean Lifetime Cost ($)	Mean Survival Time (y)	ICER ($/y)
Surgery/ablation	29,210	7.60	—
Chemoradiotherapy	46,350	7.72	142,833 (125,401;163,449)
Radiotherapy	49,400	7.08	Dominated

Future outcomes were discounted at 3%.

Deshmukh et al., Am J Clin Oncol, 2018

Figure 3. Difference in Overall Survival by Treatment



No. at risk

Chemoradiotherapy	1724	1513	1161	784
Local excision	500	419	290	161

P = .93 (log-rank test).

Pas de différence en survie globale de l'excision locale par rapport à la radio-chimiothérapie.

Chai et al., JAMA Surgery, 2018.

Critiques du traitement par excision locale.

Réponse à l'article de Chai.

"Overall survival […] for T1N0 tumors, little between-treatment differences would be expected […]. Locoregional failure is a more appropriate primary outcome, and historically, local excision for canal lesions is associated with unacceptably high recurrence rates."

Renehan et al., JAMA Oncol, 2018.

Méta-analyse systématique

Table 2: Summary of Findings: Local excision alone versus chemoradiation in early stages

Outcome	Participants (studies)	Confidence in the effect estimate (GRADE)	Relative effect (95% CI)	Absolute effects	
				Risk with chemoradiation	Risk difference with local excision
Overall survival	2,300 pts. with anal canal cancer stage I from 2 comparative cohort studies [1, 2]	⊕◯◯◯ VERY LOW [a,b]	**HR 1.07** (0.80 to 1.44)	868 per 1,000 (5-year OS)	**9 fewer per 1,000** (52 fewer to 25 more)
Progression-free survival	57 pts. with anal canal cancer stage I from 1 comparative cohort study [2]	⊕◯◯◯ VERY LOW [a,b]	**HR 0.94** (0.09 to 9.44)	830 per 1,000 (5-year PFS)	**9 more per 1,000** (658 fewer to 153 more)
Recurrence	82 pts. with anal cancer (SISCCA or Stage I) from 2 comparative cohort studies [2, 3]	⊕◯◯◯ VERY LOW [a,b,c,d]	**RR 1.26** (0.03 to 45.83)	54 per 1,000	**14 more per 1,000** (52 fewer to 2402 more)
Treatment-associated deaths	57 pts. with anal canal cancer stage I from 1 comparative cohort study [2]	⊕◯◯◯ VERY LOW [a,b]	**RR 0.46** (0.03 to 8.36)	68 per 1,000	**37 fewer per 1,000** (66 fewer to 502 more)

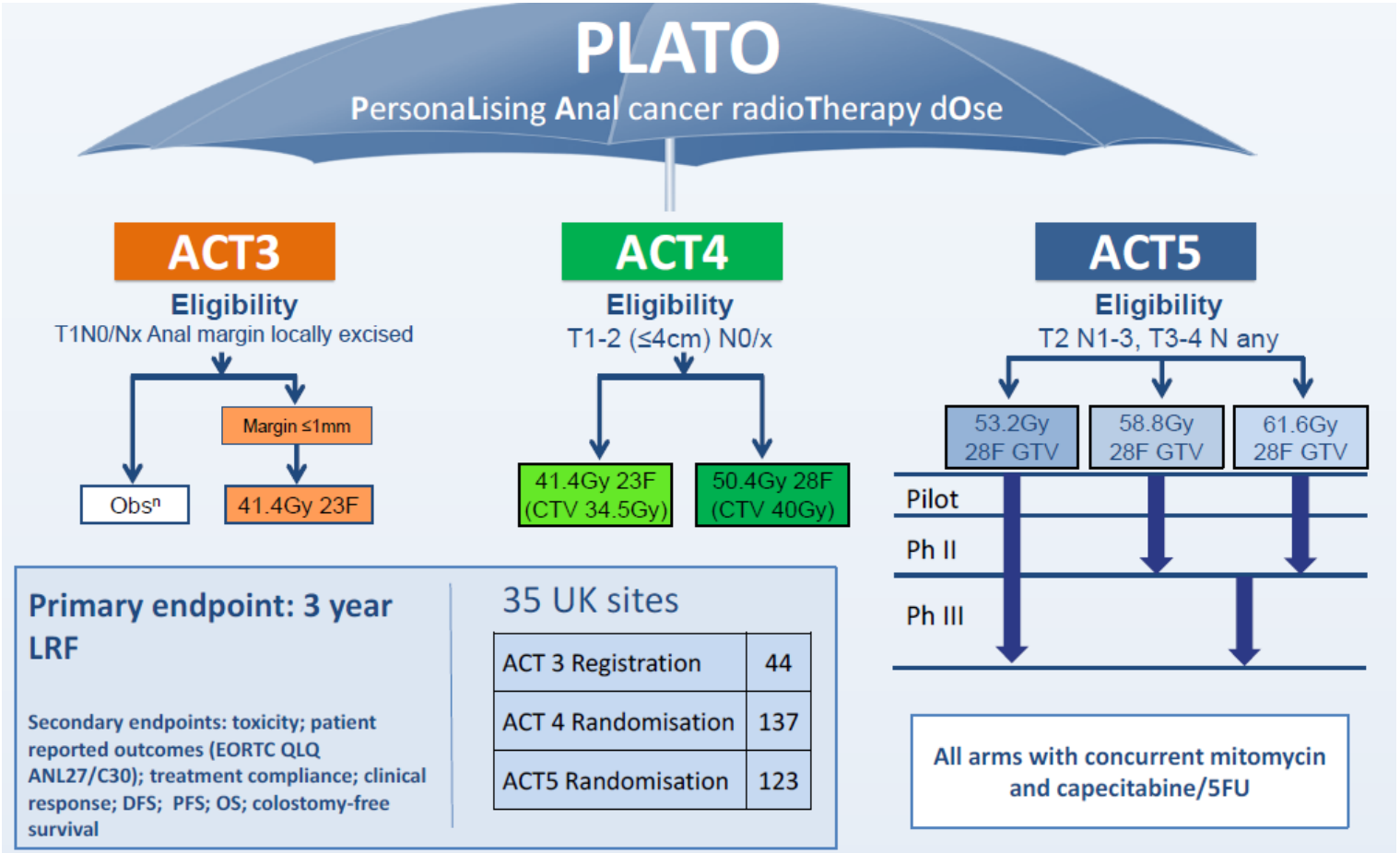
a. Risk of bias.
b. Confidence interval includes the minimally relevant difference in both directions (0.80; 1.25).
c. I^2=73%, contrary effect estimates.
d. Participants partly HIV positive.

Table 3: Summary of Findings: Local excision versus radiotherapy in early stages

Outcome	Participants (studies)	Confidence in the effect estimate (GRADE)	Relative effect (95% CI)	Absolute effects	
				Risk with radiotherapy	Risk difference with local excision
Overall survival	94 pts. >65 years with anal canal cancer stage I from 1 comparative registry-based cohort study [4]	⊕◯◯◯ VERY LOW [a]	**HR 0.46** (0.20 to 1.08)	610 per 1,000 (5-year OS) [5]	**187 more per 1,000** (24 fewer to 296 more)

a. Confidence interval includes the line of no effect (1.00) and the minimally relevant difference (0.80).

Wermer et al., Radiotherapy and Oncology, 2021



ACT3: Low risk disease – can a highly selective policy of involved field chemoradiotherapy (CRT) result in low locoregional failure (LRF) in small anal margin tumours treated by local excision?

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Locoregional disease[e] (± positive para-aortic lymph nodes)[f]	→ Mitomycin/5-FU[h] + radiation therapy (RT)[i] or Mitomycin/capecitabine[h] + RT[i] or 5-FU/cisplatin[h] + RT[i] (category 2B)	→ Follow-up Therapy and Surveillance (ANAL-3)

" The exception is small, well or moderately differentiated perianal lesions and superficially invasive lesions, which can be treated with margin-negative local excision alone."

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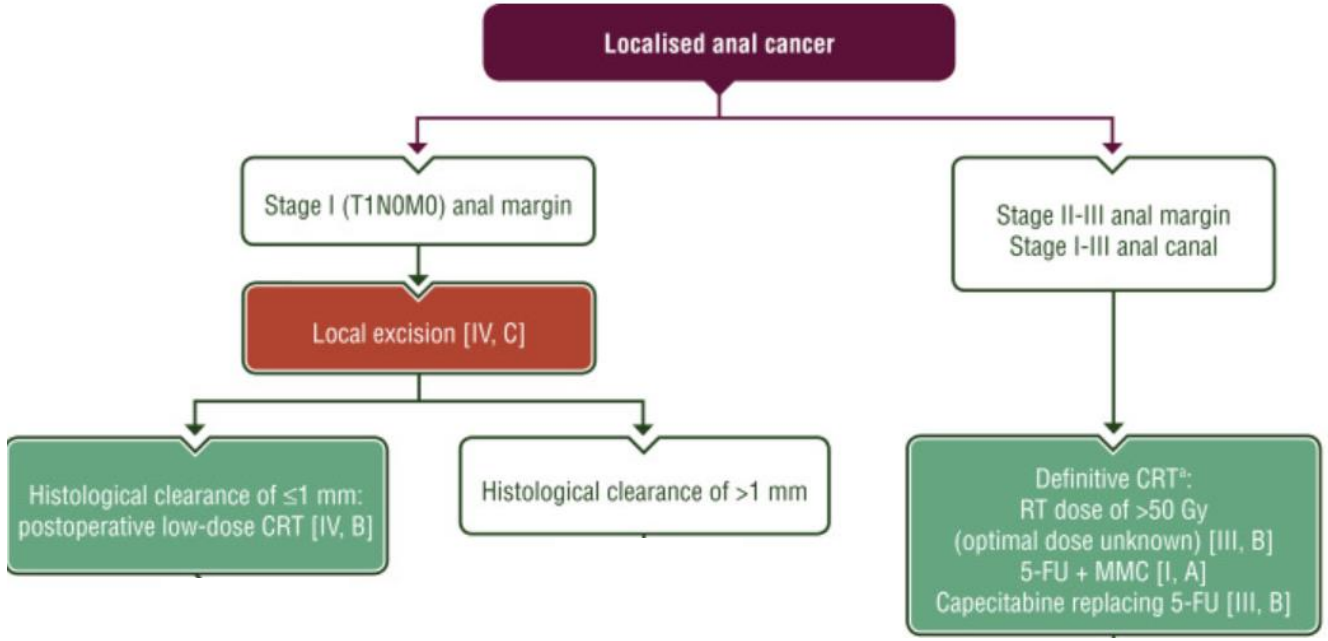
ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Anal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up☆



"Local excision of early-stage cancers in the anal canal is contraindicated."

Benson *et al.,* JNCCN, 2018 ; Rao *et al.,* Ann Oncol, 2021

- La radio-chimiothérapie est le traitement présentant le plus fort niveau de preuve dans cette population.
- La radio-chimiothérapie est source de toxicités aigues et tardives importantes.
- La radiothérapie exclusive paraît comme une option dans cette population, suffisante chez une majorité de patients.
- La radiothérapie exclusive est actuellement proposée majoritairement à des patients plus âgés.
- Sous réserve de potentiels biais, la survie pourrait être moins bonne après radiothérapie exclusive.
- L'IMRT est la principale évolution dans le traitement de ces tumeurs.
- La chirurgie d'excision locale est un traitement qui se développe.
- Actuellement, le niveau de preuve de l'efficacité oncologique de l'excision locale reste faible.
- L'excision locale s'adresse préférentiellement aux tumeurs T1N0 de la marge anale et aux lésions in situ du canal anal.
- L'excision locale doit être réservée aux situations pour lesquelles le bilan initial permet d'envisager une exérèse complète avec marge > 1 mm.

Merci pour votre attention

Centre
Eugène Marquis
RENNES