e-session 577

Updates in the diagnosis and treatment of anal cancer

Expert: **Prof Pierfrancesco Franco**, University of Eastern Piedmont, Novara, Italy

Discussant: **Dr Berardino De Bari**, Réseau Hospitalier Neuchâtelois, La Chaux-de-Fonds, Switzerland

e-ESO – Live session 17.06.2021

Updates in the diagnosis and treatment of anal cancer

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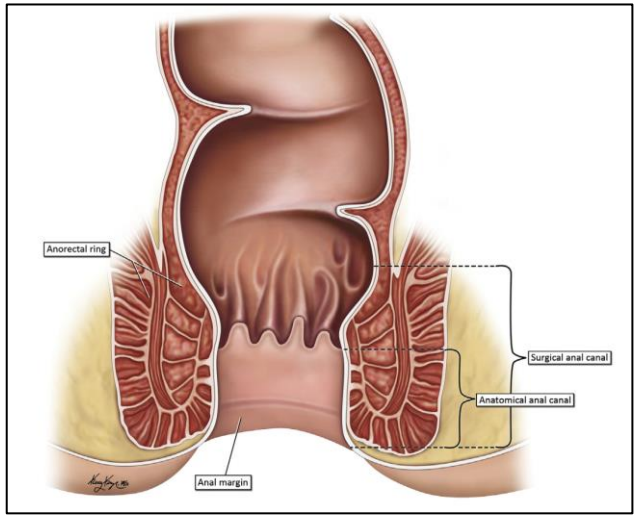
Dipartimento di Radioterapia Oncologica, AOU 'Maggiore della Carità', Novara

Outline

- ✓Epidemiology and risk factors
- ✓Diagnosis
- ✓Treatment
  - ✓Radiation
  - ✓Combination therapy
- ✓Follow up and QoL

General points



Courtesy of Kage KM, MDACC, Houston, Tx

Anal canal

- Tumor arising within the mucosa-lined anal canal 1-2 cm proximal to the dentate line to the intersphinteric groove separating the anal margin to the anal canal

Anal margin

- Skin within 5 cm radius to the anal verge

- 1-3 new cases/100.000 in Western Countries
- Rare cancer (<6 new cases/100.000 persons/year)
- Growing incidence (both male and female)
- 2% of all GI tract tumors
- F:M ratio = 1.5/2; F: anal canal; M: anal margin
- < 35 yrs higher in male population
- Median age at diagnosis: 60 yrs

TABLE 3. Incidence (Cases, Age-Standardized Rate, Cumulative Risk) and Mortality (Deaths, ASR, Cumulative Risk) for 36 Cancers and All Cancers Combined (Including Nonmelanoma Skin Cancer) by Sex in 2018

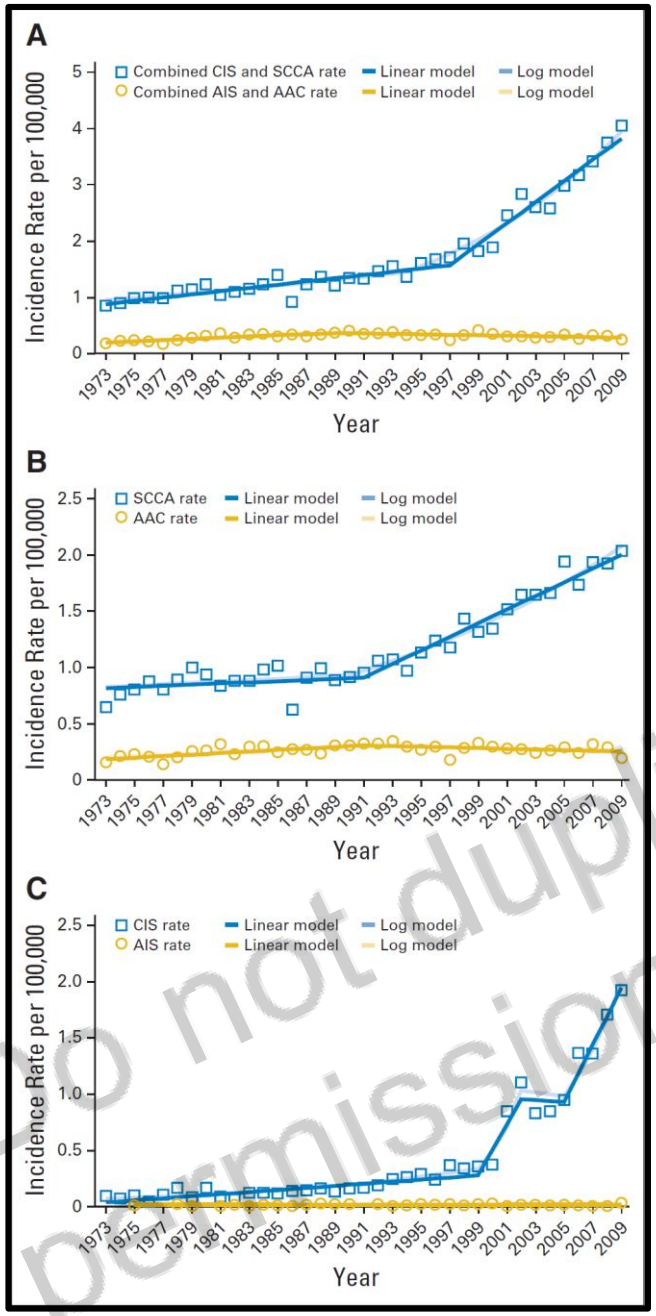
	INCIDENCE						MORTALITY					
	MALES			FEMALES			MALES			FEMALES		
CANCER SITE	CASES	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	CASES	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	DEATHS	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	DEATHS	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %
Lip, oral cavity	246,420	5.8	0.66	108,444	2.3	0.26	119,693	2.8	0.32	57,691	1.2	0.14
Salivary glands	29,256	0.7	0.07	23,543	0.5	0.05	13,440	0.3	0.03	8,736	0.2	0.02
Oropharynx	74,472	1.8	0.21	18,415	0.4	0.05	42,116	1.0	0.12	8,889	0.2	0.02
Nasopharynx	93,416	2.2	0.24	35,663	0.8	0.09	54,280	1.3	0.15	18,707	0.4	0.05
Hypopharynx	67,496	1.6	0.19	13,112	0.3	0.03	29,415	0.7	0.08	5,569	0.1	0.01
Esophagus	399,699	9.3	1.15	172,335	3.5	0.43	357,190	8.3	1.00	151,395	3.0	0.36
Stomach	683,754	15.7	1.87	349,947	7.0	0.79	513,555	11.7	1.36	269,130	5.2	0.57
Colon	575,789	13.1	1.51	520,812	10.1	1.12	290,509	6.4	0.66	260,760	4.6	0.44
Rectum	430,230	10.0	1.20	274,146	5.6	0.65	184,097	4.2	0.46	126,297	2.4	0.26
Anus	20,196	0.5	0.05	28,345	0.6	0.07	9,618	0.2	0.03	9,511	0.2	0.02
Liver	596,574	13.9	1.61	244,506	4.9	0.57	548,375	12.7	1.46	233,256	4.6	0.53
Gallbladder	97,396	2.2	0.25	122,024	2.4	0.26	70,168	1.6	0.17	94,919	1.8	0.19
Pancreas	243,033	5.5	0.65	215,885	4.0	0.45	226,910	5.1	0.59	205,332	3.8	0.41
Larynx	154,977	3.6	0.45	22,445	0.5	0.06	81,806	1.9	0.23	12,965	0.3	0.03
Lung	1,368,524	31.5	3.80	725,352	14.6	1.77	1,184,947	27.1	3.19	576,060	11.2	1.32
Melanoma of skin	150,698	3.5	0.39	137,025	2.9	0.31	34,831	0.8	0.08	25,881	0.5	0.05
Nonmelanoma of skin	637,733	13.9	1.31	404,323	7.0	0.67	38,345	0.8	0.08	26,810	0.5	0.04
Mesothelioma	21,662	0.5	0.05	8,781	0.2	0.02	18,332	0.4	0.04	7,244	0.1	0.02
Kaposi sarcoma	28,248	0.7	0.06	13,551	0.3	0.03	13,117	0.3	0.03	6,785	0.2	0.01
Breast				2,088,849	46.3	5.03				626,679	13.0	1.41
Vulva				44,235	0.9	0.09				15,222	0.3	0.03
Vagina				17,600	0.4	0.04				8,062	0.2	0.02
Cervix uteri				569,847	13.1	1.36				311,365	6.9	0.77
Corpus uteri				382,069	8.4	1.01				89,929	1.8	0.21

GLOBOCAN 2018 – Global cancer statistics

Courtesy of Kage KM, MDACC, Houston, Tx

Bray F et al; CA Cancer J Clin 2018

Increasing incidence



VOLUME 31 · NUMBER 12 · APRIL 20 2013
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Changing Patterns of Anal Canal Carcinoma in the United States

Rebecca A. Nelson, Alexandra M. Levine, Leslie Bernstein, David D. Smith, and Lily L. Lai

SCC

- Slope of incidence rates increases from 1997
- Annual percent change: 7.2% (men: 9.5%; woman: 4.5%)
- Rising incidence: all stages, sex and racial groups

ADK

Stable incidence

Reasons

- Longer survival for HIV pts due to highly effective HAART
- Increased exposure to HPV infection

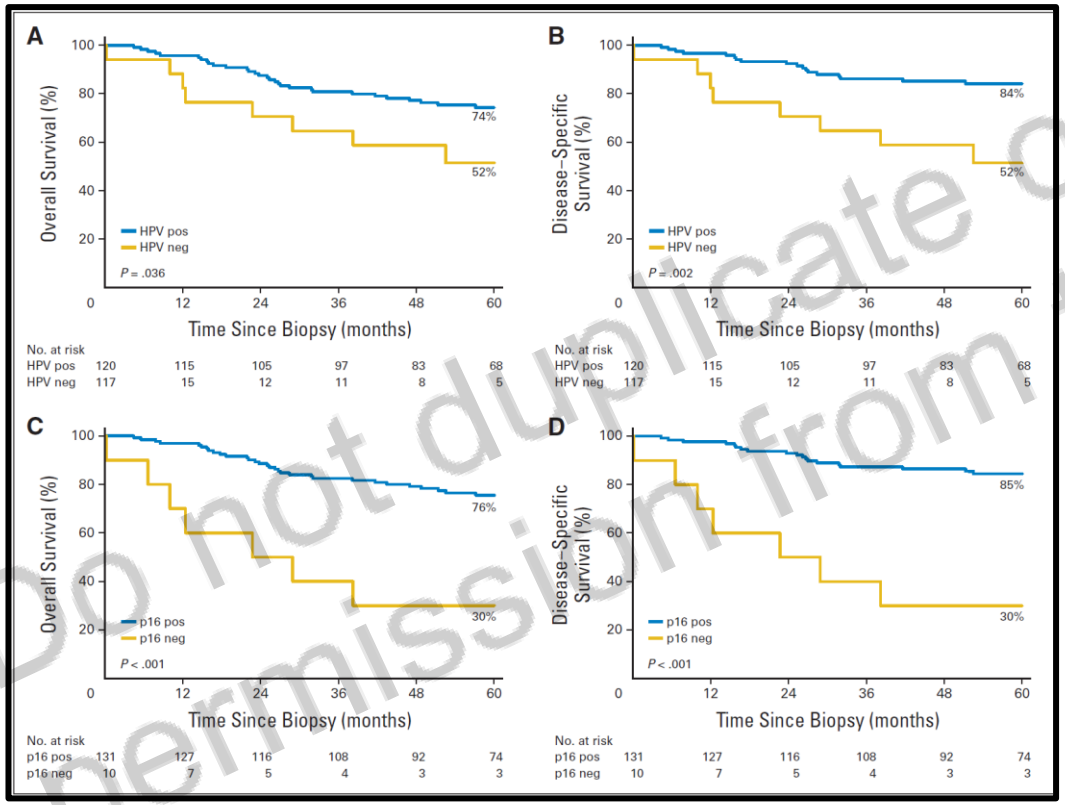
Nelson R et al; JCO 2013

HPV-related anal SCC

VOLUME 32 · NUMBER 17 · JUNE 10 2014
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Human Papillomavirus Genotyping and p16 Expression As Prognostic Factors for Patients With American Joint Committee on Cancer Stages I to III Carcinoma of the Anal Canal

Eva Serup-Hansen, Dorte Linnemann, Wojciech Skovrider-Ruminski, Estrid Høgdall, Poul Flemming Geertsen, and Hanne Havsteen



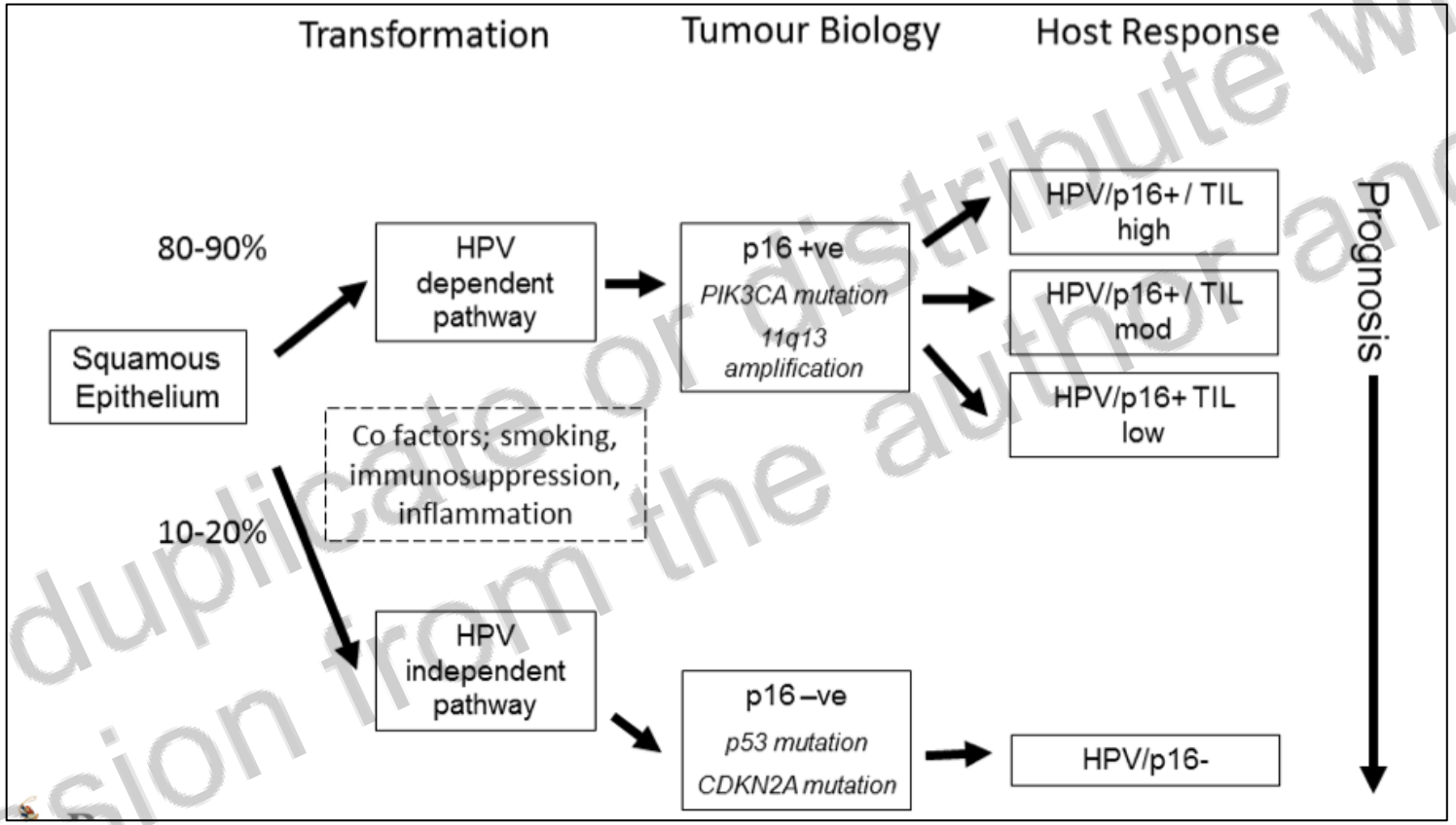
143 patients
HPV genotyping PCR:
- HPV16 (81%)
- HPV33 (5.1%)
- HPV18 (2.2%)
- HPV58 (0.7%)

p16: +ve (92.9%)

Multivariable Cox analysis:
p16 positivity – indipendent prognostic factor for both OS and DSS (HR: 0.07)

Serup-Hansen et al; JCO 2014

HPV-related anal SCC – Towards a biological model



Jones et al Br J Cancer 2017

ORIGINAL CONTRIBUTION

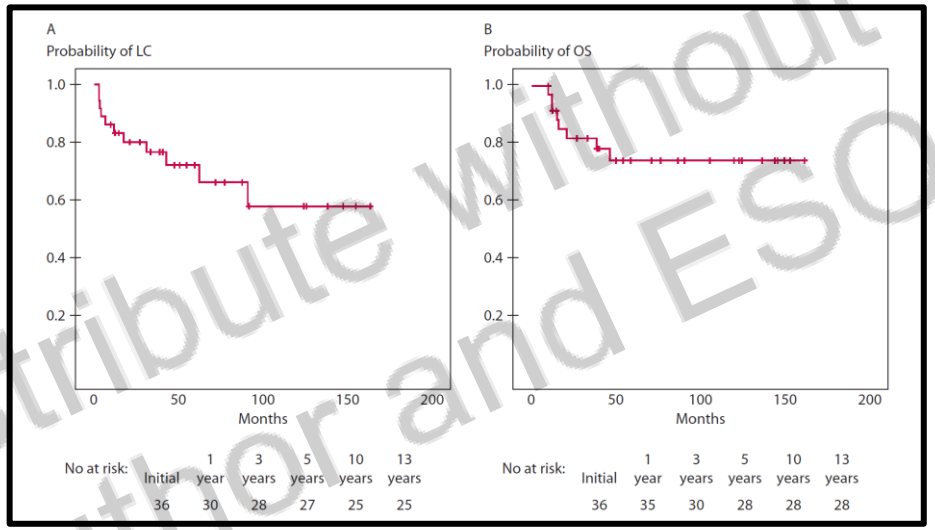
Long-term Effects of Chemoradiotherapy for Anal Cancer in Patients With HIV Infection: Oncological Outcomes, Immunological Status, and the Clinical Course of the HIV Disease

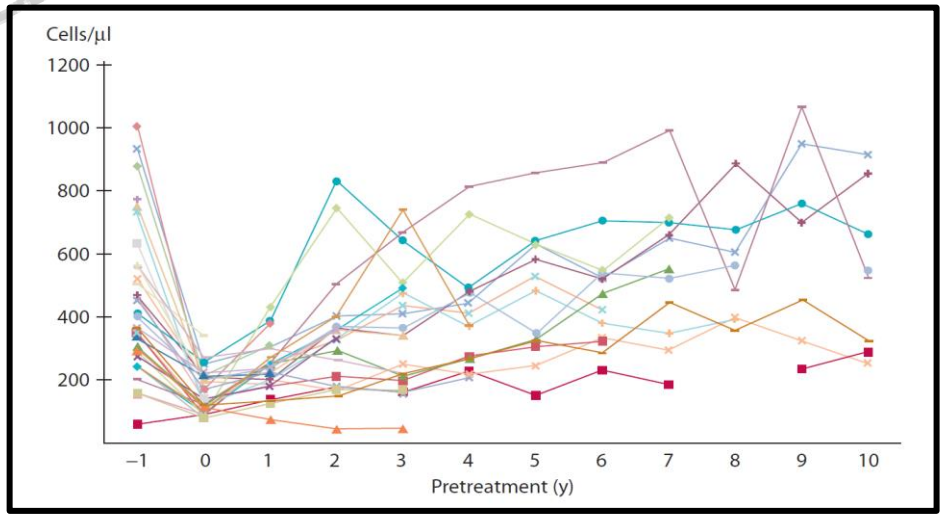
Ingeborg B. Fraunholz, M.D.[1] • Annette Haberl, M.D.[2] • Stephan Klauke, M.D.[3]
Peter Gute, M.D.[3] • Claus M. Rödel, M.D.[1]

1 Department of Radiation Oncology, Johann Wolfgang Goethe-University, Frankfurt/Main, Germany
2 HIV Treatment & Clinical Research Unit, Department of Internal Medicine II, Johann Wolfgang Goethe-University, Frankfurt/Main, Germany
3 Infectiologicum, Frankfurt/Main, Germany

TABLE 2. Number of patients experiencing acute toxicities (n = 36) (CTCAE version 4.0)

Toxicity	*Grade 1*	*Grade 2*	*Grade 3*	*Grade 4*
Dermatitis	6 (17)	15 (42)	10 (28)	0
Diarrhea	15 (42)	7 (19)	1 (3)	0
Nausea/vomiting	8 (22)	4 (11)	0	0
Proctitis	5 (14)	3 (8)	1 (3)	0
Urinary frequency/urgency	9 (25)	0	0	0
Pain caused by CRT	4 (11)	10 (28)	2 (6)	0
Blood/bone marrow				
Hemoglobin	5 (14)	6 (17)	1 (3)	0
Leukocytes	9 (25)	7 (19)	11 (31)	1 (3)
Platelets	7 (19)	6 (17)	3 (8)	1 (3)





- Highly active antiretroviral therapy era: HIV +ve anal cancer patients treated with RT-CT have good clinical outcomes
- RT-CT induced decline in CD4 counts is persistent but is not associated to increased clinical morbidity

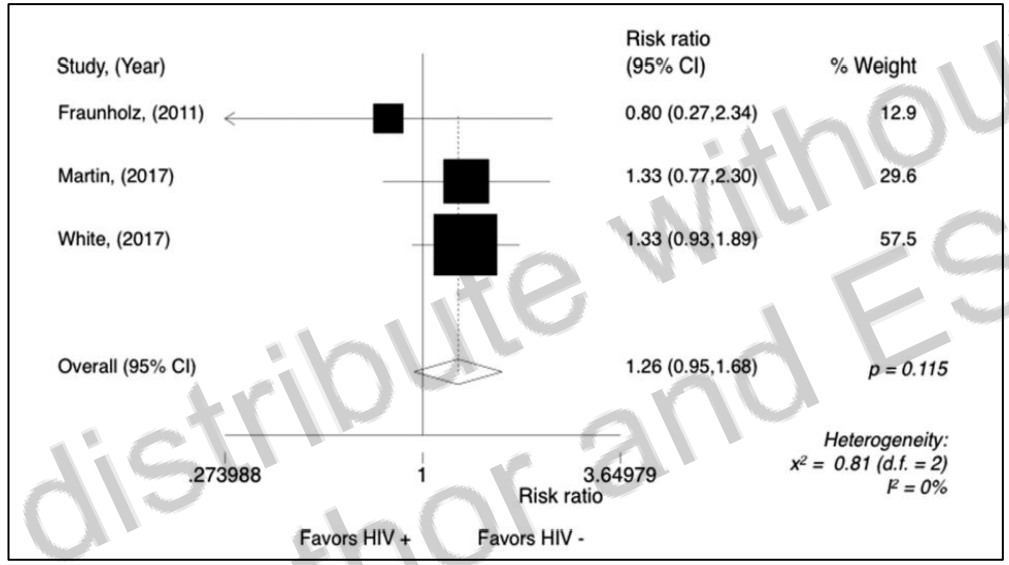
Fraunholz et al ; Dis Colon Rectum 2014

Original Article

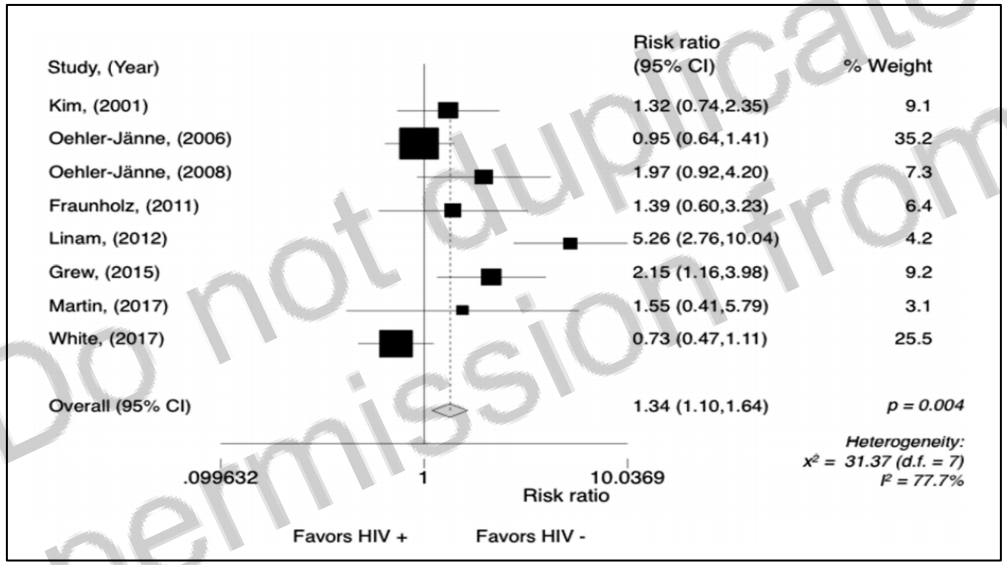
Treatment outcomes of patients with localized anal squamous cell carcinoma according to HIV infection: systematic review and meta-analysis

Marcos Pedro Guedes Camandaroba[1], Raphael Leonardo Cunha de Araujo[2,3], Virgílio Souza e Silva[1], Celso Abdon Lopes de Mello[1], Rachel P. Riechelmann[1]

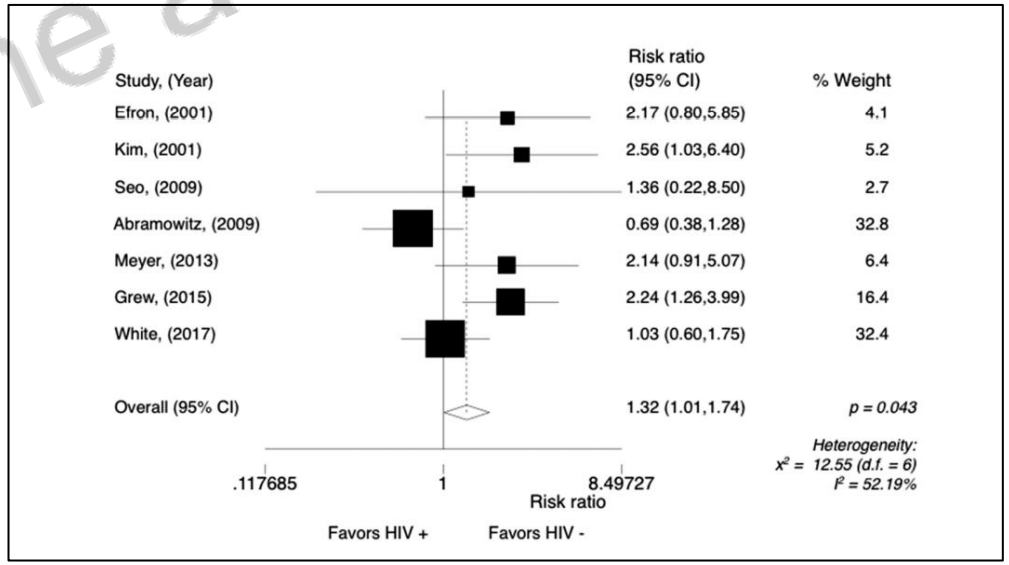
Forest plot of G3/4 leukopenia in comparative studies



Forest plot of G3/4 cutaneous toxicities in comparative studies



Forest plot of disease free survival rate at 3 years in comparative studies



Camandaroba MPG et al ; J Gastrointest Oncol 2019

IMACC Visual Abstract

Global registry on clinical outcomes of HIV-infected patients with anal cancer

HIV+ve patients are underrepresented in trials of SCCA.[1]

Studies by our group suggest HIV+ve have:

- **inferior disease-free and overall survival rates following chemoradiation for localized disease. [2]**
- **Longer time to CR [3]**
- **In the metastattic setting, their OS seem equivalent to HIV-ve patients.[4]**

Hence, more data are needed to understand how to best manage these patients

Global retrospective and prospective cohort of HIV-infected patients with SCCA of any stage.

Main endpoints:

-localized SCCA: 6-months complete response rate after chemorads and disease-free survival rates at 2 years

-metastatic: overall survival

- **Outcomes according to Nigro vs ACT-II regimens, by stage, by region/country**
- **Treatment regimens**
- **Results to be compared historically to data from RCT/large series (mostly HIV-ve)**

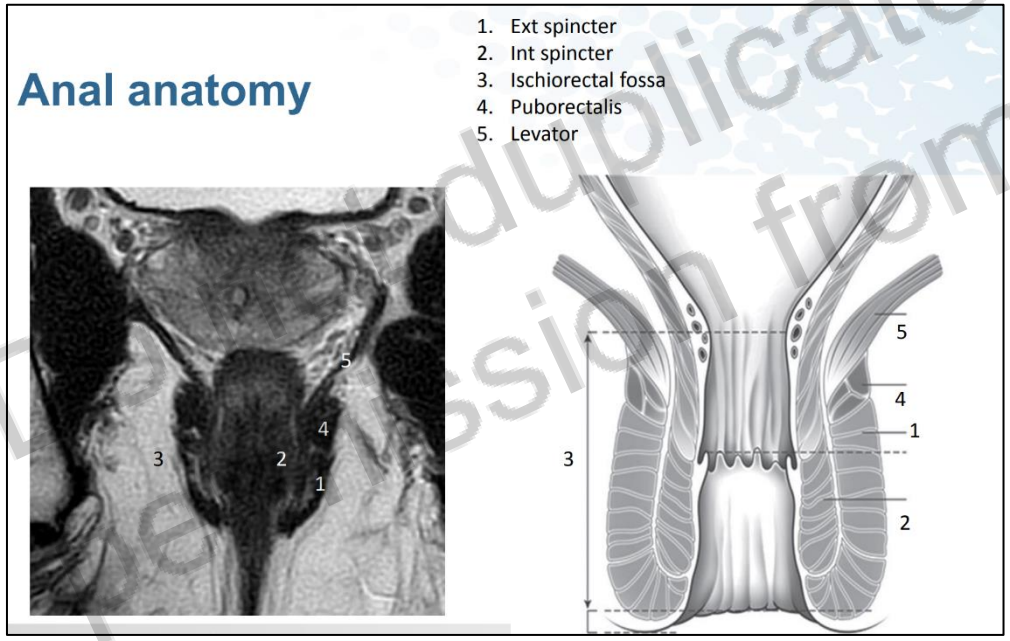
1- Donadio, Riechelmann. .Ecancermedicalscience. 2020 May 7;14:1037
2- Camandaroba & Riechelmann. J Gastrointest Oncol. 2019 Feb;10(1):48-60
3- Camandaroba & Riechelmann. Clin Colorectal Cancer. 2020 Sep;19(3):e129-e136
4- Raphaeli & Riechelmann. ESMO pôster pres. 2020

Prof. Dr. Rachel Riechelmann
Director of Clinical Oncology, AC Camargo Cancer Center, Sao Paulo, Brazil
President: Brazilian GI Tumors
Rachel.riechelmann@accamargo.org.br

Magnetic Resonance Imaging

MRI technique and tips

- ✓ ESGAR 2016 guidelines
- ✓ No fat sat
- ✓ 3T or 1.5T Phased-array surface coil
- ✓ T2w axial pelvis
- ✓ T2w sag, axial oblique, coronal oblique (spinchter) 3 mm
- ✓ DWI – b0,b800,b1500
- ✓ Reporting Template



MRI Anal Squamous Cell Cancer Baseline Staging Template
SAR Rectal/Anal Cancer DFP 2019_v1
CLINICAL INFORMATION: [FREE TEXT]
(Note: Use this template squamous cell anal cancer; do NOT use not for adenocarcinoma of the rectum involving the anal canal)
TECHNIQUE: [FREE TEXT]
COMPARISON:
FINDINGS:
TUMOR SIZE: [ ] cm x [ ] cm (largest measurement in any plane x perpendicular measurement)
T-STAGE:
□ Tx/T0 (primary tumor cannot be assessed/no MR evidence of primary tumor)
□ T1 (≤ 2 cm)
□ T2 (> 2 cm and ≤ 5 cm)
□ T3 (> 5 cm)
□ T4* (tumor of any size invading adjacent organ(s), NOT including sphincter, rectal wall, skin, subcutaneous tissue)
*Structures with invasion/possible invasion: [None/FREE TEXT]
FUNCTIONAL SEQUENCES:
DWI:
□ Restricted diffusion
□ No restricted diffusion
□ N/A
LYMPH NODES*: *[locoregional*: internal iliac/obturator, external iliac, mesorectal, inguinal, superior rectal/hemorrhoidal]
□ N0: No visible or no suspicious regional lymph nodes
□ N1a: Suspicious inguinal, mesorectal AND/OR internal iliac lymph node(s)
□ N1b: Suspicious external iliac lymph node(s)
□ N1c: Suspicious external iliac AND any N1a lymph node (inguinal, mesorectal, or internal iliac)
OTHER: [FREE TEXT other pelvic organs, bones, other incidental findings]
IMPRESSION:
1. [FREE TEXT] 2. mr T [ ] N [ ]

Courtesy Soren Rafaelson @IMACC2020 webinar

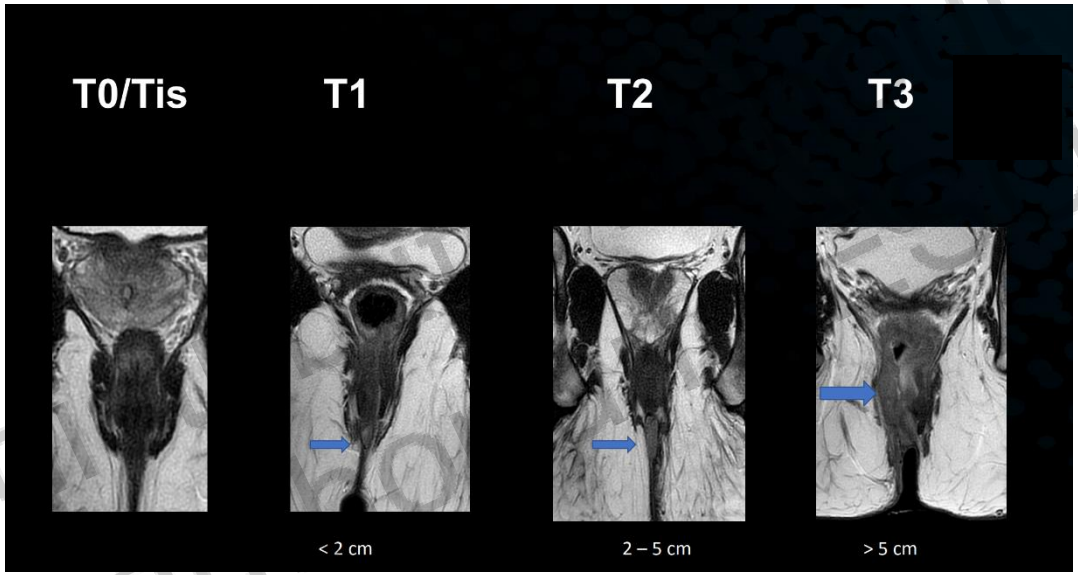
Magnetic Resonance Imaging

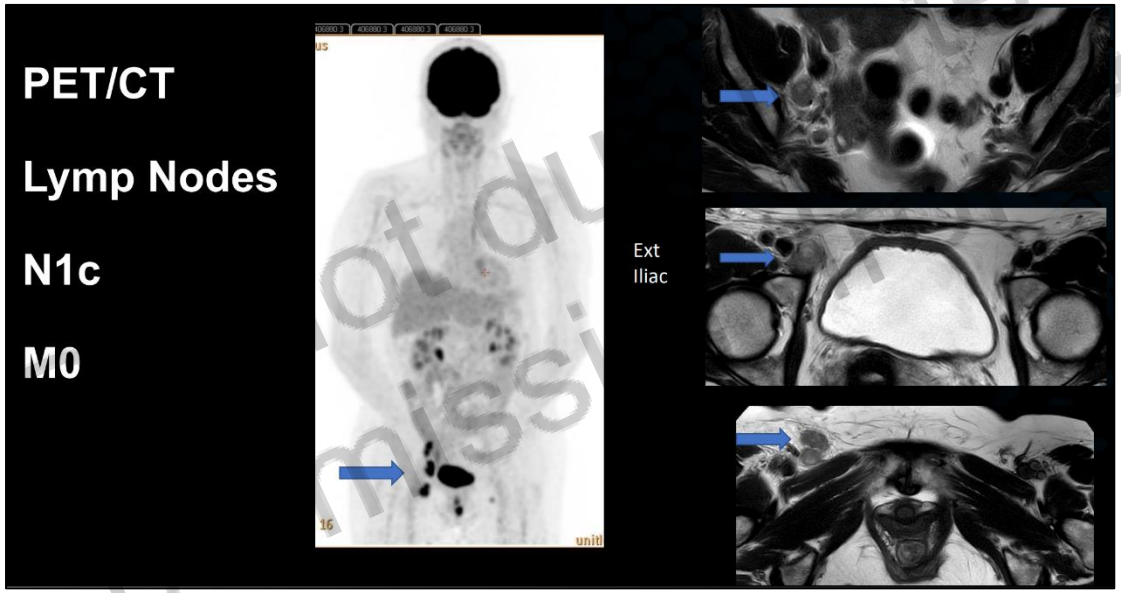
SAR suggested criteria for lymph node staging

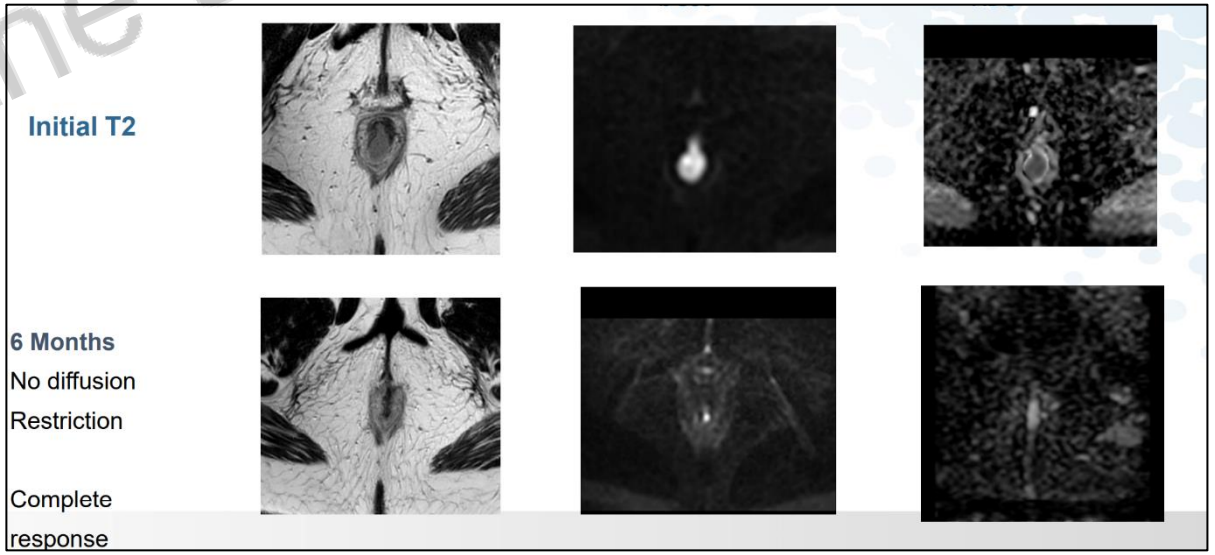
- Mesorectal and superior rectal:
- ≥ 9 mm short axis diameter
- 5-8 mm short axis diameter and 2 morphological suspicious characteristics*
- < 5 mm short axis diameter and 3 morphological suspicious characteristics*
- Internal iliac and obturator:
- ≥ 5 mm short axis diameter
- Inguinal lymph nodes
- ≥ 1 cm short axis diameter
- External and common iliac nodes:
- ≥ 1 cm short axis diameter

* *Round shape, Irregular border, Heterogeneous signal*

Marc J. Gollub
ESGAR 2019







Courtesy Soren Rafaelson @IMACC2020 webinar

Magnetic Resonance Imaging

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Clinical Oncology xxx (xxxx) xxx

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journal homepage: www.clinicaloncologyonline.net

A Prospective Study of Diffusion-weighted Magnetic Resonance Imaging as an Early Prognostic Biomarker in Chemoradiotherapy in Squamous Cell Carcinomas of the Anus

R. Muirhead [*], D. Bulte [†], R. Cooke [‡], K.-Y. Chu [‡§], L. Durrant [‡§], V. Goh [¶], C. Jacobs [*], S.M. Ng [‖], V.Y. Strauss [**], P.S. Virdee [**], C. Qi [**], M.A. Hawkins [‡]

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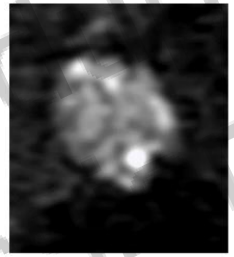
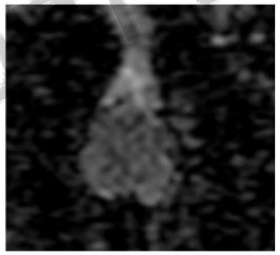
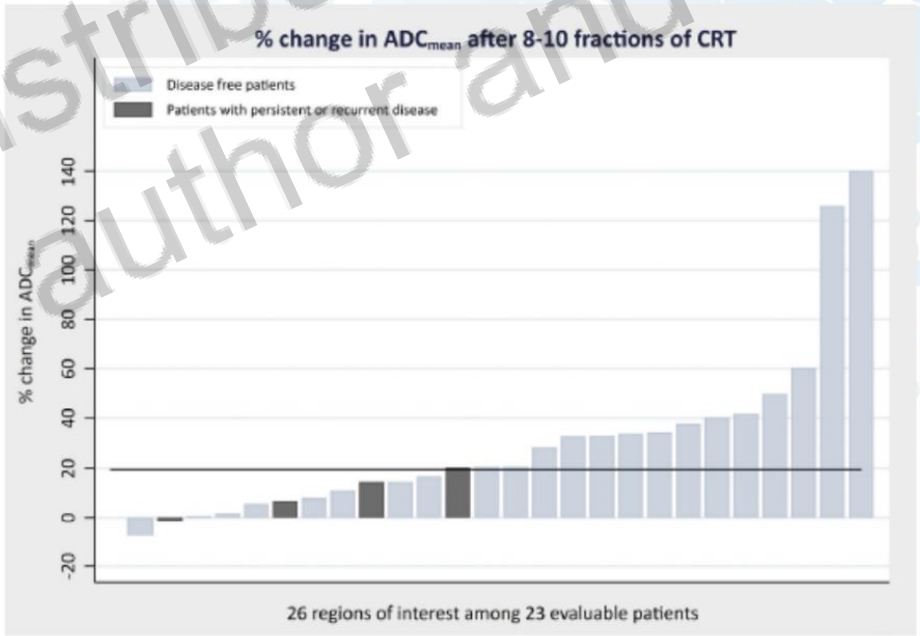
[‖] Oncology Clinical Trials Office, Department of Oncology, University of Oxford, Oxford, UK
[**] Centre for Statistics in Medicine, NDORMS, University of Oxford, Oxford, UK

DWI b800



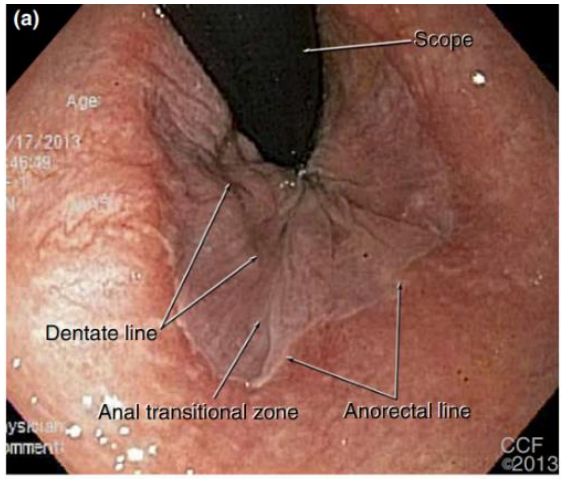
ADC Map





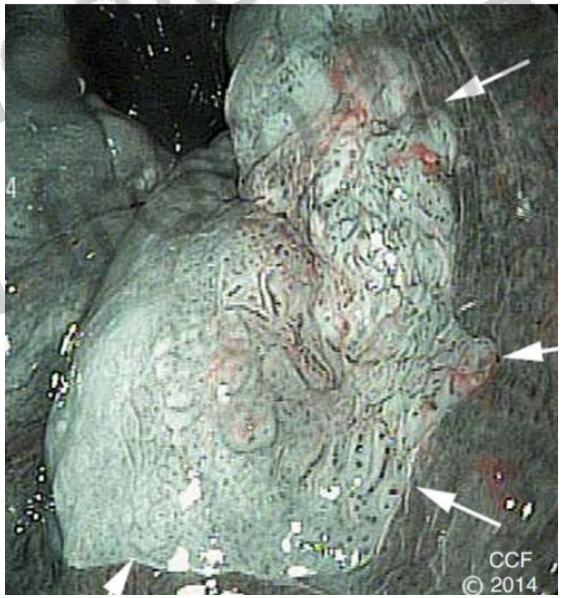
The authors demonstrated a potential correlation between patients with ΔADCmean <20% and disease relapse.

Narrow Band Imaging (NBI)

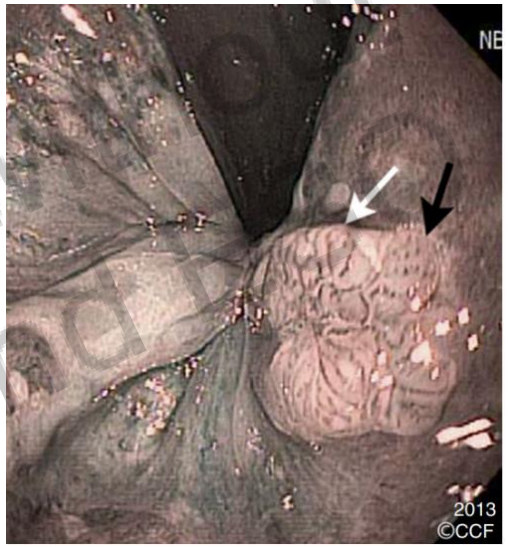


The anal transitional zone is located between the dentate line and anorectal line. (b) Retroflexion with white light shows the dentate line, the anal transitional zone and the anorectal line

NBI is an optical technology which helps to visualize the minutest vascular and mucosal patterns. NBI uses only wavelengths absorbed by hemoglobin for maximum contrast. Compared to white-light endoscopy, the images of capillaries are less blurred and the probability of missing a lesion is reduced.



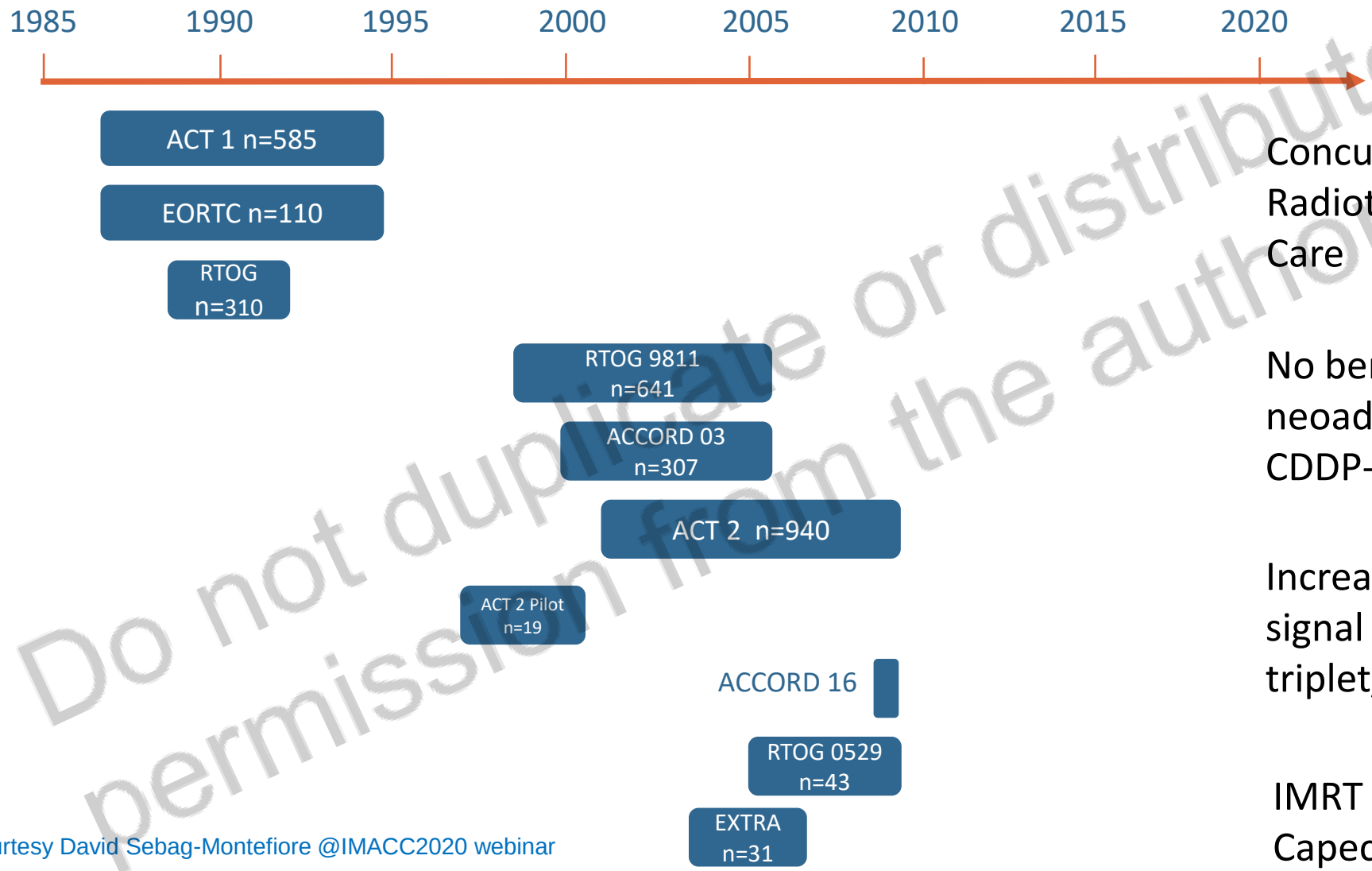
Examination with NBIA revealed a complex collection of slightly raised lesions with enhanced vascularity. Multiple lesions (see arrows) not visible with white light are seen on retroflexion. All lesions were ablated with hot biopsy forceps. Pathology showed HSIL.



Anal transitional zone lesion in the left anterior position illuminated with NBI. Note the enhanced punctation (black arrow) and mosaicism (white arrow). Figure shows a left anterior raised lesion with punctation and mosaicism;pathology showed HSIL.

Inkster MD et al ; Colorectal Dis 2015

Treatment of squamous cell carcinoma of the anus



Courtesy David Sebag-Montefiore @IMACC2020 webinar

Concurrent MMC 5FU and Radiotherapy is Standard of Care

No benefit from addition of neoadjuvant or maintenance CDDP-5FU

Increased toxicity and no signal of benefit with triplet/EGFR

IMRT
Capecitabine

First generation trials in anal cancer: oncologic outcomes and toxicity profile

		Disease-related outcomes			Acute toxicities				Late toxicities
Trial	**Comparison**	**5-year LR-control**	**5-year OS**	**5-year CFS**	**Hematol**	**Skin**	**GI**	**GU**	**Skin + GI + GU + others**
ACT I	RT + 5-FU/MMC vs RT alone	68% vs 43%	58% vs 53%	47% vs 37%	Leukopenia: 7% vs 0% Thrombocitopenia: 5% vs 0%	Severe: 17% vs 14%	Severe: 5% vs 2%	1% vs 0%	Skin: 21% vs 18% Anorectal:29%vs27% GU: 4% vs 4% Ulcers/radionecrosis: 8% vs 6%
EORTC 22861	RT + 5-FU/MMC vs RT alone	68% vs 51%	58% vs 53%	72% vs 40%	NR	G3-G4: 60% vs 50%	G3-G4 diarrhea: 20% vs 8%	NR	Skin ulceration: 6% vs 4%

Glynne-Jones et al – Surg Oncol Clin N Am 2017

Second generation trials in anal cancer: oncologic outcomes and toxicity profile

		Outcomes		Acute toxicity			Late toxicity		
Trial	**Comparison**	**LR control**	**DFS CFS OS**	**Hematol**	**Skin**	**GI GU**	**Skin**	**GI GU**	**Other**
RTOG 87-04	RT + 5-FU/MMC vs RT + 5-FU	84% vs 66% 4-years	73% vs 51% 76% vs 67% 71% vs 59%	G4-G5: 18% vs 3%	Non hematologic toxicity – G4-G5: 7% vs 4%		G4-G5 late toxicity: 5% vs 1%		
RTOG 98-11	RT + 5-FU/MMC vs ICT (5-FU/DDP) + RT and conc 5-FU/DDP	80% vs 74% 5-years	68% vs 58% 78% vs 71% 72% vs 65%	G3-G4: 62% vs 42%	G3-G4: 49% vs 41%	G3-G4:37%vs47% G3-G4:3%vs3%	G3-G4: 4%vs2 %	G3-G4: 3%vs2%	Total G3-G4: 13%vs11%
ACCORD 03	ICT (5-FU/DDP) + RT and 5-FU/DDP vs RT and conc 5-FU/DDP	80% vs 81% 5-years	72% vs 65% 72% vs 65% 77% vs 75%	G3-G4: 19% vs 12% (during RT-CT)	G3-G4: 3% vs 3% (mucositis)	G3-G4:9%vs11% (diarrhea during RT-CT)	NR	G3-G4: Diarrhea -5% Incontinence :15% Ulceration/fistula: 12%	G3-G4: Bleeding:25 % Anal pain:12%
ACT II	RT + 5-FU/MMC vs RT + 5-FU/DDP + maintainance DDP	NR	69% vs 69% 79% vs 77% 68% vs 67%	G3-G4: 26% vs 16%	G3-G4: 48% vs 47%	G3-G4:16%vs18% G3-G4:1%vs2%	NR	NA	NA

Glynne-Jones et al – Surg Oncol Clin N Am 2017

Radiotherapy and Oncology 117 (2015) 240–245

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Anal cancer

Chemoradiotherapy for squamous cell carcinoma of the anal canal: Comparison of one versus two cycles mitomycin-C

Evan C. White *, Kelly Goldman, Alexey Aleshin, Winston W. Lien, Aroor R. Rao

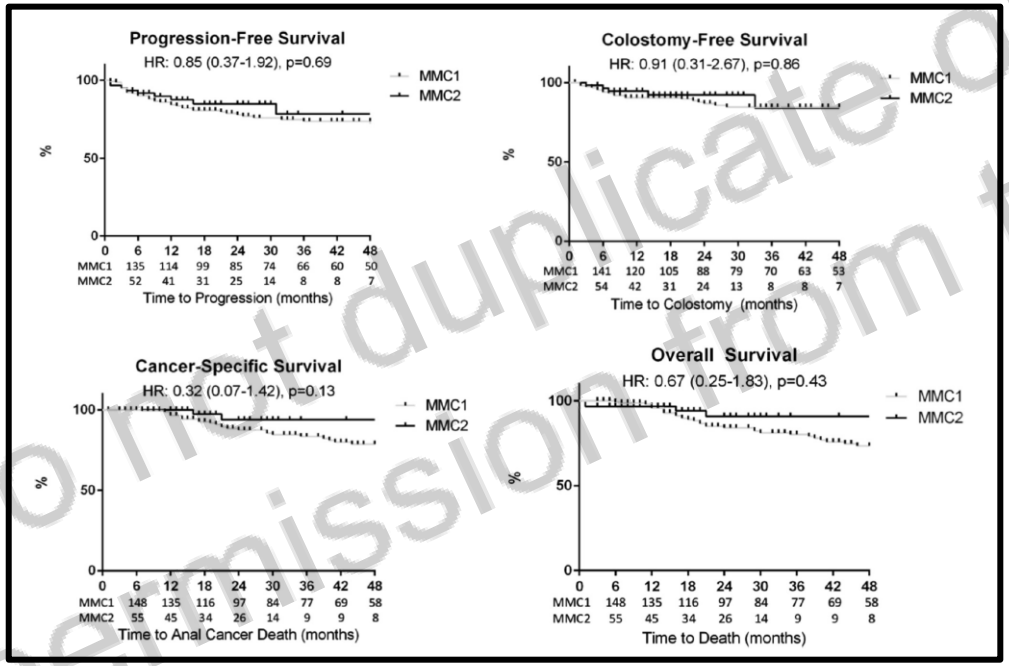
Department of Radiation Oncology, Kaiser Permanente Southern California, Los Angeles Medical Center, United States

MMC: 1 vs 2 cycles

- 217 pts
  - MMC x 1 cycle(154 pts)
  - MMC x 2 cycles (63 pts)

No significant difference in:
PFS, CFS, CSS, OS

Lower rate of ≥G2 acute toxicity with MMC x 1 cycle



	MMC1 (N = 154)	MMC2 (N = 63)	P value
(a) Acute toxicity			
Grade ⩾3 overall	65 (42)	26 (41)	1
Grade ⩾2 heme			
Overall hematologic	113 (73)	56 (89)	**0.01**
Leukopenia	104 (68)	54 (86)	**0.01**
Neutropenia	82 (53)	45 (71)	**0.02**
Anemia	53 (34)	29 (46)	0.12
Thrombocytopenia	42 (27)	21 (33)	0.41
Grade ⩾2 skin	129 (84)	61 (97)	**0.006**
Grade ⩾2 GI	94 (61)	42 (67)	0.54
Grade ⩾2 GU	13 (8)	12 (19)	**0.04**
Hospitalization during treatment	26 (17)	13 (21)	0.56
Radiation treatment break	45 (29)	12 (19)	0.13
Treatment related death	0 (0)	3 (5)	**0.02**
(b) Late toxicity			
Any late toxicity	72 (47)	27 (43)	0.65
Late grade ⩾3 toxicity	11 (7)	3 (5)	0.76
Late grade ⩾2 toxicity	50 (32)	14 (22)	0.14

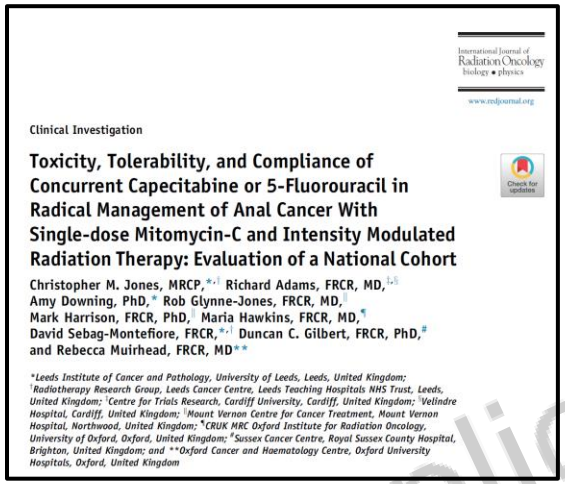
White et al; Radiother Oncol 2015

Oral fluoropyrimidines

Study	N° of pts	RT dose	MMC schedule	Cape	LC
Glynne-Jones et al (2008)	31	50.4Gy/28fr in 2 phases	12 mg/m^2 single dose (max: 20 mg/m2)	825 mg/m2 bid on RT days	90% at 14 months
Deenen et al (2013)	18	59.4Gy/33fr with SIB-IMRT	10 mg/m^2 single dose (max: 15 mg/m2)	825 mg/m2 bid on RT days	88% at 28 months
Olivera et al (2016)	51	NA	15 mg/m^2 single dose (d1)	825 mg/m2 bid on RT days	86% at 6 months
Thind et al (2014)	66	Median dose: 51.9 Gy over 5.5 weeks	12 mg/m^2 single dose (d1)	825 mg/m2 bid on RT days	94% at 20 months
Wan et al (2014)	300	50-54 Gy	2 doses; poor compliance with cape	825 mg/m2 bid on RT days	1-year DFS: 94% (Cape) vs 91% (5-FU)

Glynne-Jones et al – Surg Oncol Clin N Am 2017

Capecitabine vs 5-FU in combination with MMC



International Journal of Radiation Oncology biology • physics

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Clinical Investigation

Toxicity, Tolerability, and Compliance of Concurrent Capecitabine or 5-Fluorouracil in Radical Management of Anal Cancer With Single-dose Mitomycin-C and Intensity Modulated Radiation Therapy: Evaluation of a National Cohort

Christopher M. Jones, MRCP,*,† Richard Adams, FRCR, MD,‡,§ Amy Downing, PhD,* Rob Glynne-Jones, FRCR, MD,‖ Mark Harrison, FRCR, PhD,‖ Maria Hawkins, FRCR, MD,¶ David Sebag-Montefiore, FRCR,*,† Duncan C. Gilbert, FRCR, PhD,# and Rebecca Muirhead, FRCR, MD**

*Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, United Kingdom; †Radiotherapy Research Group, Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; ‡Centre for Trials Research, Cardiff University, Cardiff, United Kingdom; §Velindre Hospital, Cardiff, United Kingdom; ‖Mount Vernon Centre for Cancer Treatment, Mount Vernon Hospital, Northwood, United Kingdom; ¶CRUK MRC Oxford Institute for Radiation Oncology, University of Oxford, Oxford, United Kingdom; #Sussex Cancer Centre, Royal Sussex County Hospital, Brighton, United Kingdom; and **Oxford Cancer and Haematology Centre, Oxford University Hospitals, Oxford, United Kingdom

Similar levels of overall G3/G4 toxicity Capecitabine/MMC vs 5-FU/MMC

Different toxicity pattern with less hematologic toxicity with capecitabine/MMC

Table 4 Comparison of grade 3 and 4 toxicity between the 2 groups

Variable	MMC/capecitabine (n = 47, nonhematologic; n = 48, hematologic)	MMC/5-FU (n = 71, nonhematologic; n = 66, hematologic)	*P* value	IPTW *P* value*
Any grade 3/4 toxic effect†	21 (45)	39 (55)	.35	.19
Nonhematologic†,‡	20 (43)	30 (42)	1.00	.72
Gastrointestinal	8 (17)	9 (13)	.60	.72
Nausea	1 (2)	3 (4)	1.00	.39
Vomiting	1 (2)	2 (3)	1.00	.7
Diarrhea	8 (17)	5 (7)	.60	.12
Stomatitis	0 (0)	3 (4)	.16	-
Other	0 (0)	1 (1)	1.00	-
Skin	12 (26)	20 (28)	.83	.71
Anal pain	9 (19)	6 (9)	.10	.1
Cardiac	2 (4)	1 (1)	.56	-
Other	2 (4)	4 (6)	1.00	.2
Hematologic†,§	2 (4)	18 (27)	.001‖	<.001‖
WBC count	1 (2)	13 (20)	.004‖	<.001‖
Platelet count	0 (0)	9 (14)	.01	NA
Hemoglobin	1 (2)	1 (2)	1.00	.82
Febrile neutropenia	1 (2)	0 (0)	.42	NA

Abbreviations: 5-FU = 5-fluorouracil; IPTW = inverse probability of treatment weighting; MMC = mitomycin C; WBC = white blood cell.
Data presented as n (%).

* *P* values shown for statistical analyses undertaken using Fisher exact test and after IPTW; treatment groups were balanced for the following baseline characteristics: age, sex, presence of pretreatment colostomy, primary tumor site, and T stage; we could not obtain estimates for toxicity subgroups with a small number of events or no events in 1 of the treatment groups.

† Patients who experienced >1 toxic effect were counted once at the highest grade recorded.

‡ At an α value of 0.05, a Bonferroni-adjusted *P* value < .0046 was considered statistically significant to account for multiple significance testing.

§ At an α value of 0.05, a Bonferroni-adjusted *P* value < .01 was considered statistically significant to account for multiple significance testing.

‖ Statistically significant.

Jones et al – IJROBP 2018

EGFR inhibition

Trial	N° of pts	IMRT	Regimen	Toxicity	Efficacy
Olivatto et al – Phase I (2013)	21 (stopped for DLT)	No	5-FU/CP + RT + Cet	High	Acceptable
ACCORD 16 (Deutsch et al 2013; Levy et al 2015)	16 (stopped for DLT)	No	5-FU/CP + RT + Cet	High	Low
ECOG3205 – Phase I (Garg et al 2012)	28	Some	5-FU/CP + RT + Cet	G4: 32% G5: 4%	2-year OS: 93%
Garg et al – Phase II (2016)	45	Some	5-FU/CP + RT + Cet	G4: 26% G5: 4%	2-year OS: 89%
Leon et al – Phase I (ASCO 2015)	13	Yes	5-FU/CP + RT + Cet	Low	2-year CR rate: 73%
Feliu et al- Phase II (ASCO 2014)	58 (36 evaluable)	No	5-FU/CP + RT + Pani	High	2-year CR rate: 55%

Glynne-Jones et al – Surg Oncol Clin N Am 2017

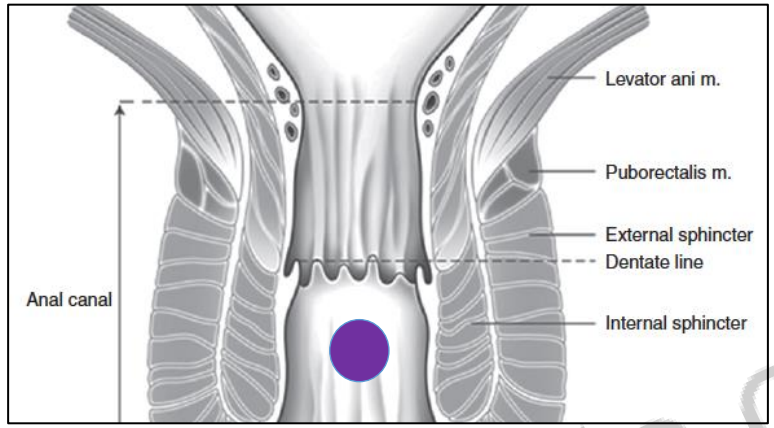
Which dose to prescribe in anal cancer patients ?

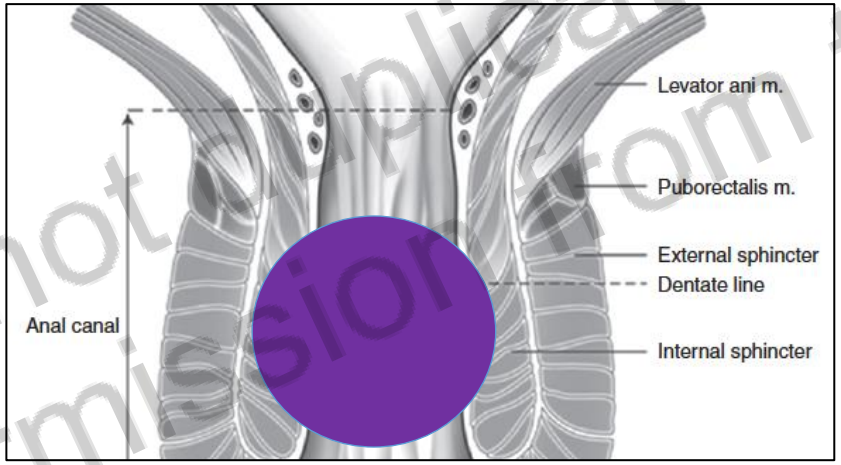
	ESMO-ESSO-ESTRO	NCCN	French Intergroup	UK
T1-T2 N0	50-50.4 Gy in 25-28 fr	45 Gy in 25 fr (only T1N0)	36-45 Gy in 20-25 fr + boost 15 Gy	50.4 Gy in 28 fr
T3-T4 or any T, N+	50-50.4 Gy + Boost (dose not specified)	45 Gy/25fr + boost 9-14 Gy (including T2N0)	36-45 Gy in 20-25 fr + boost 15-25 Gy	53.2 Gy in 28 fr

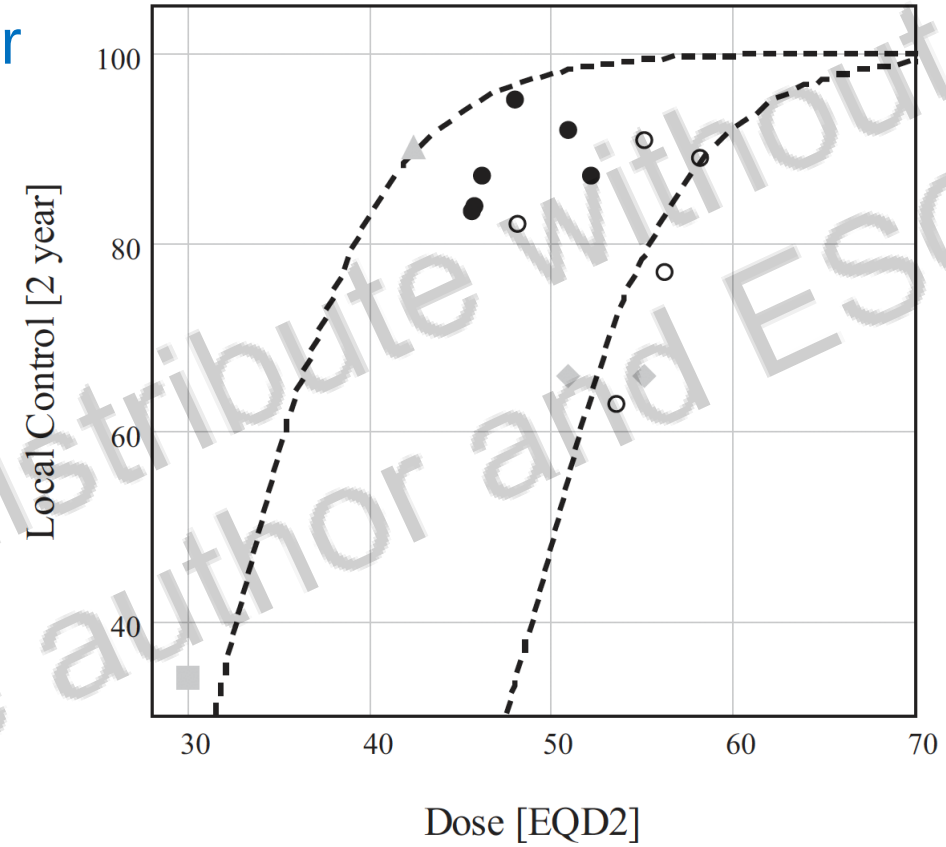
Heterogeneity in dose prescription

Glynne-Jones et al Ann Oncol 2014; Benson JNCCN 2018; Moureau-Zabotto et al; Dig Liver Dis 2017; Muirhead et al UK Guidelines 2016

Local tumor control probability in anal cancer



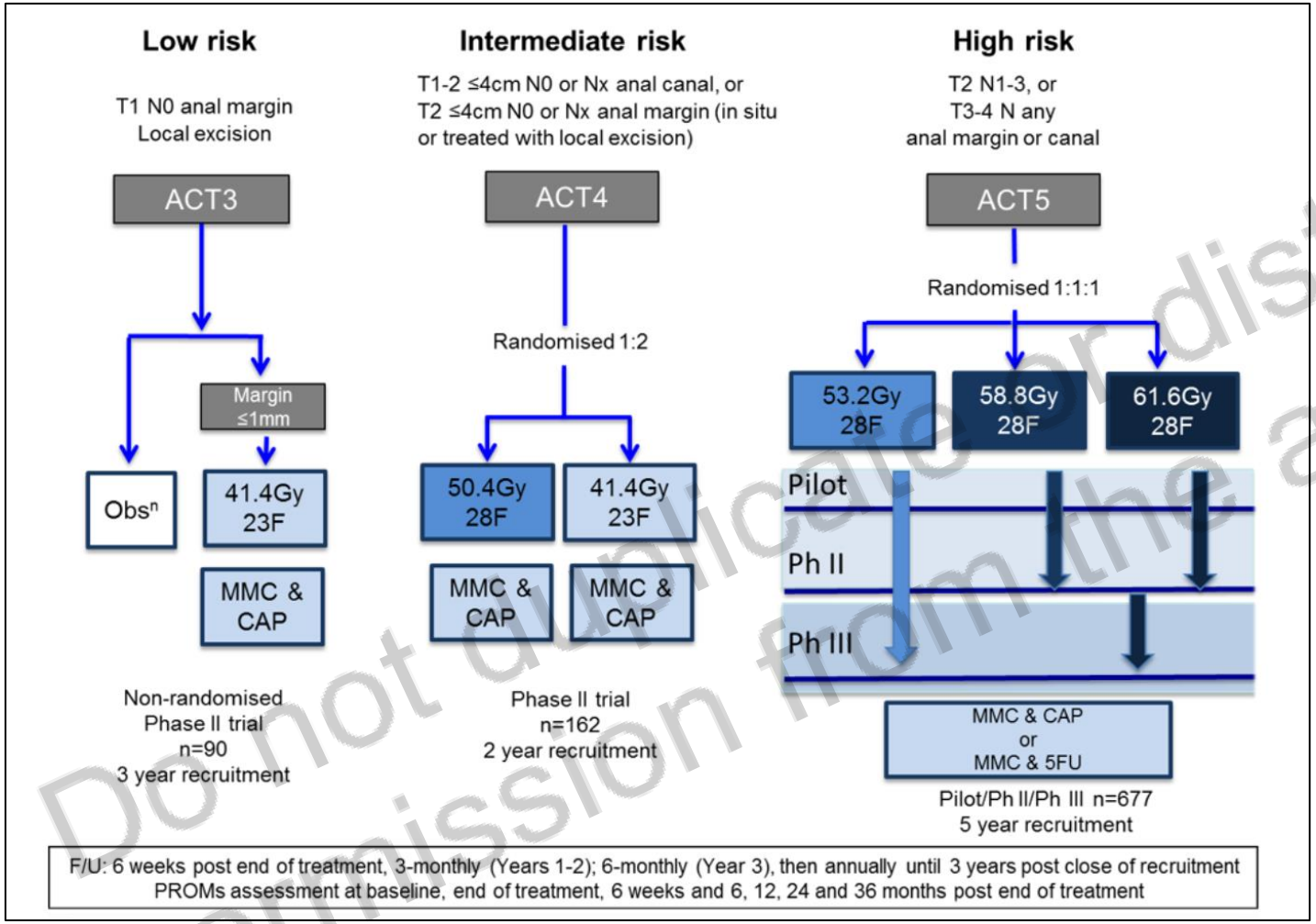




- Early stage disease: 5 Gy decrease in dose (from 50 Gy to 45 Gy) – 2-year LC reduced from 98% to 95%
- Advaced stage disease: 5 Gy increase in dose (from 50 Gy to 55 Gy) – 2-year LC reduced from 80% to 50%

Muirhead et al; Radiother Oncol 2015
Johnson et al Radiother Oncol 2018

PLATO trials: PersonaLising Anal cancer radioTherapy dOse



ACT3: for small anal margin lesions treatable by local excision, does highly selective lower-dose CRT result in low rate of locoregional failure (LRF)?

ACT4: for early stage disease, does lower dose CRT result in an acceptably low rate of LRF and reduced acute and late toxicity

ACT5: for locally advanced anal cancer, does dose-escalated CRT using IMRT result in a significant reduction in LRF with acceptable acute and late toxicity?

EA 2182: De-Intensified ChemoRadiation for Early-Stage Anal SqCell Cancer (DECREASE)

ECOG-ACRIN cancer research group
Reshaping the future of patient care

n=14

Inclusion:

-T1-T2 N0 M0 ≤ 4cm

- N0 by PET/CT and pelvic CT/MRI criteria

- HIV negative or positive (CD4 > 200)

Design:

- *n* = 252

- Stratified by T1 vs. T2 and HIV status

R
1:2

Standard-Dose Chemoradiation

- GTV: **50.4 Gy in 28 fractions**
- CTV: 42 Gy in 28 fractions
- MMC D 1; 5-FU CI X 2 cycles or Capecitabine

De-intensified Chemoradiation

- GTV:
  T1: 36.0 Gy in 20 fractions
  T2: 41.4 Gy in 23 fractions
- CTV:
  T1: 32 Gy in 20 fractions
  T2: 34.5 Gy in 23 fractions
- MMC D 1; 5-FU CI X 1 cycle OR Capecitabine

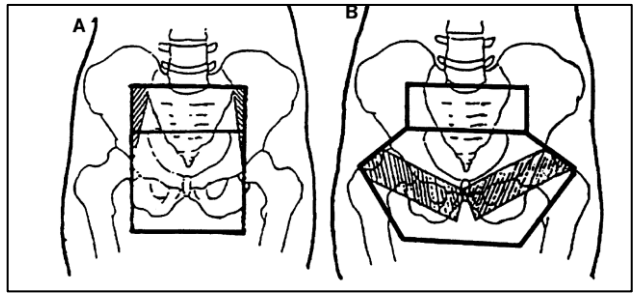
Co-Primary Objective:

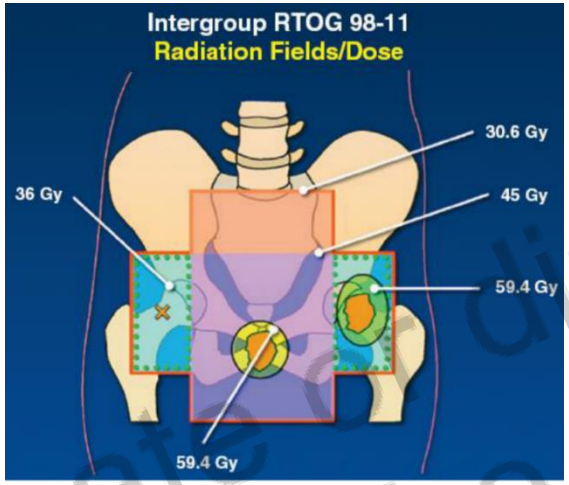
- De-intensified CRT to achieve 2-year Disease Control ≥ 85%
- Improvement in anorectal HRQoL (FIQoL coping/behavior domain)

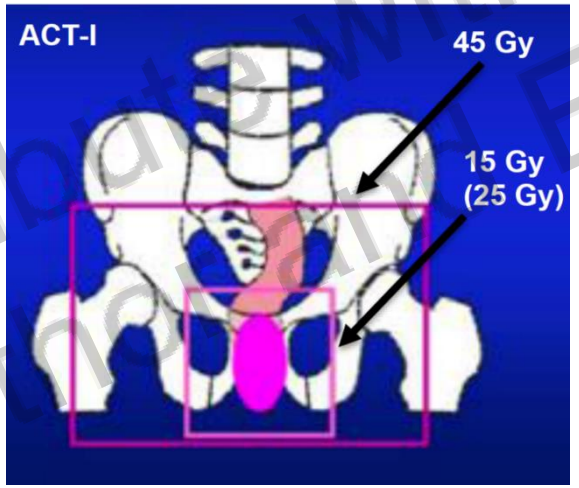
Slide courtesy of Jenny Dorth and Josh Meyer

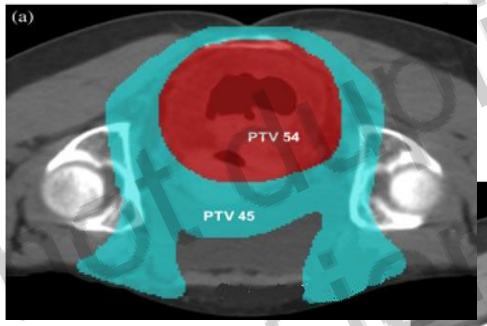
Anal SCC: varibility in treatment volume definition and selection

RTOG 87-04

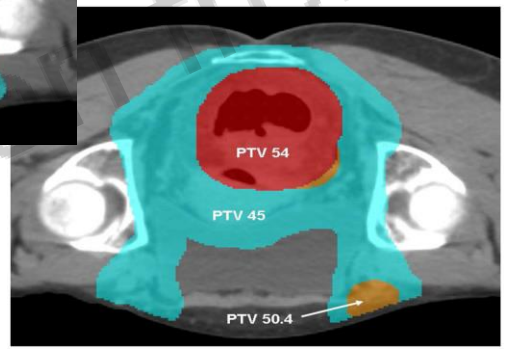


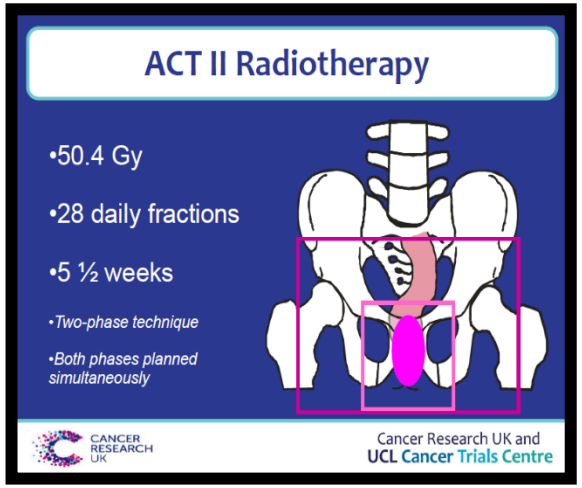






RTOG 05-29





Flam M et al JCO 1996 Ajani JA et al, JAMA 2008 Kachnich L et al, IJROBP UKCCR, Lancet 1996 James RD, Lancet Oncol 2013

IMRT in anal cancer

			G3-G4 acute tocixity (%)			
Studies	**Notes**	**Pts**	**Hematol**	**Skin**	**GI**	**GU**
Prospective trials						
RTOG 98-11	3DCRT + 5-FU/MMC arm	325	62	49	37	3
RTOG 0529	IMRT + 5-FU/MMC	52	58	23	21	3
Single-arm IMRT series						
Milano et al (2005)	Retrospective	17	53	0	0	0
Salama et al (2007)	Retrospective	53	59	38	15	0
Pepek et al (2010)	Retrospective	29	24	0	16	3
DeFoe et al (2012)	Retrospective	78	13	29	28	NR
Kachnic et al (2012)	Retrospective	43	51	10	7	7
Viellot et al (2012)	Retrospective	39	27	42	10	5
Han et al (2014)	Retrospective	58	41	46	9	0
Janssen et al (2014)	Retrospective	25	19	24	0	0
Mitchell et al (2014)	Retrospective	65	3	17	9	2
Belgioia et al (2015)	Retrospective	41	5	5	7	0
Franco et al (2015)	Retrospective	54	17	13	8	2

Comparator

IMRT series

Ludmir et al – Surg Oncol Clin N Am 2017

Comparative data

Studies	Notes	Pts	Hematol	Skin	GI	GU
Saarilahti et al (2008)	3DCRT vs IMRT Retrospective	39 vs 20	NR	82 vs 80	31 vs 0	35 vs 7
Bazan et al (2011)	3DCRT vs IMRT Retrospective	17 vs 29	29 vs 21	41 vs 21	29 vs 7	NR
Dewas et al (2012)	3DCRT vs IMRT Retrospective	27 vs 24	4 vs 4	35 vs 38	4 vs 4	NR
Choung et al (2013)	3DCRT vs IMRT Retrospective	37 vs 52	38 vs 29 Leukopenia	65 vs 12	30 vs 10	5 vs 0
Koerber et al (2014)	3DCRT vs IMRT Retrospective	37 vs 68	NR	95 vs 63 (G2-G3)	68 vs 47 (G2-G3)	NR

Ludmir et al – Surg Oncol Clin N Am 2017

Clinical series – a growing evidence for IMRT

ACTA ONCOLOGICA, 2016
VOL. 55, NO. 6, 767–773
http://dx.doi.org/10.3109/0284186X.2015.1120886

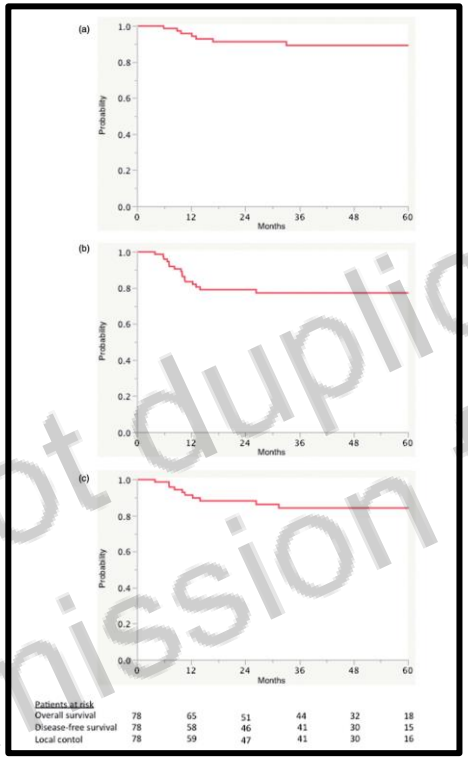
Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Efficacy and safety of helical tomotherapy with daily image guidance in anal canal cancer patients

Berardino De Bari[a], Raphael Jumeau[a], Hasna Bouchaab[b], Véronique Vallet[c], Oscar Matzinger[a], Idriss Troussier[a], René-Olivier Mirimanoff[a], Anna Dorothea Wagner[b], Dieter Hanhloser[d], Jean Bourhis[a] and Esat Mahmut Ozsahin[a]

[a]Radiation Oncology Department, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; [b]Medical Oncology Department, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; [c]Medical Physics, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; [d]Surgery Department, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.



5-year:
- ❑ LC: 84.2%
- ❑ DFS: 77.2%
- ❑ CFS: 89.3%
- ❑ OS: 89.3%

De Bari et al et al – Acta Oncol 2016

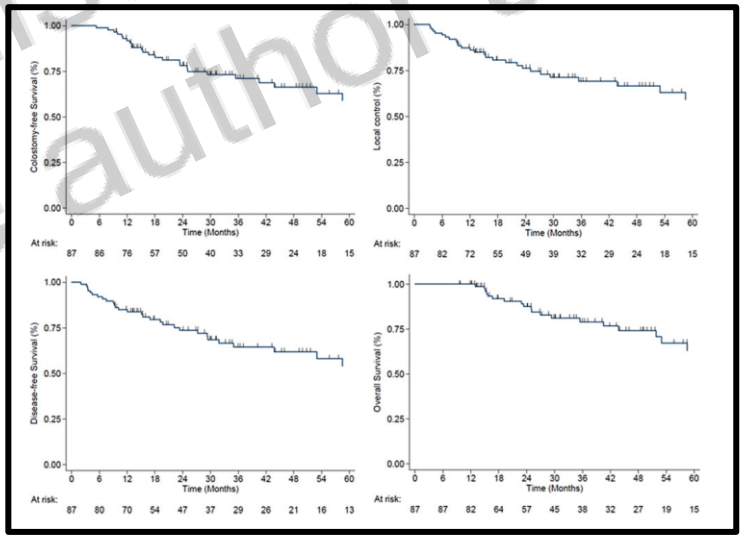
Received: 21 June 2017 | Revised: 2 August 2017 | Accepted: 2 August 2017
DOI: 10.1111/ajco.12768

ORIGINAL ARTICLE

WILEY

Image-guided IMRT with simultaneous integrated boost as per RTOG 0529 for the treatment of anal cancer

Francesca Arcadipane[1] | Pierfrancesco Franco[1] | Manuela Ceccarelli[2] | Gabriella Furfaro[1] | Nadia Rondi[1] | Elisabetta Trino[1] | Stefania Martini[1] | Giuseppe Carlo Iorio[1] | Massimiliano Mistrangelo[3] | Paola Cassoni[4] | Patrizia Racca[5] | Mario Morino[2] | Umberto Ricardi[1]



3-year:
- ❑ LC: 69%
- ❑ DFS: 71%
- ❑ CFS: 64%
- ❑ OS: 79%

Arcadipane et al et al – APJCO 2018

SIB – RTOG 0529 protocol

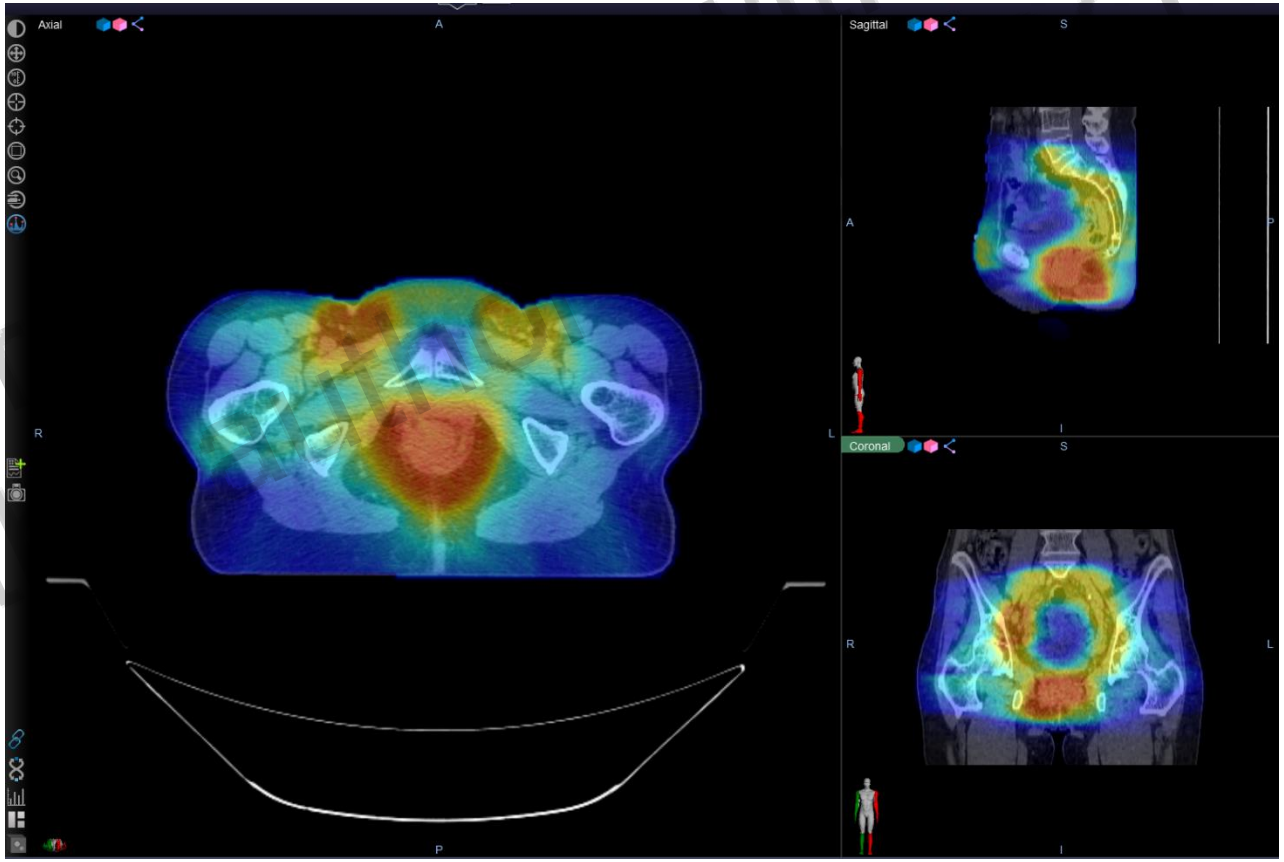
Radiotherapy Dose Prescription (RTOG 0529)
Macroscopic disease – 54/50.4 Gy in 30 fractions (1.8–1.68 Gy per fraction) during 6 weeks
Elective volumes – 45 Gy in 30 fractions (1.5 Gy per fraction) in 6 weeks

Based on SIB approach

PTV 1: 54 Gy/30fr
PTV 2: 50,4 Gy/30fr
PTV 3: 45 Gy/30fr

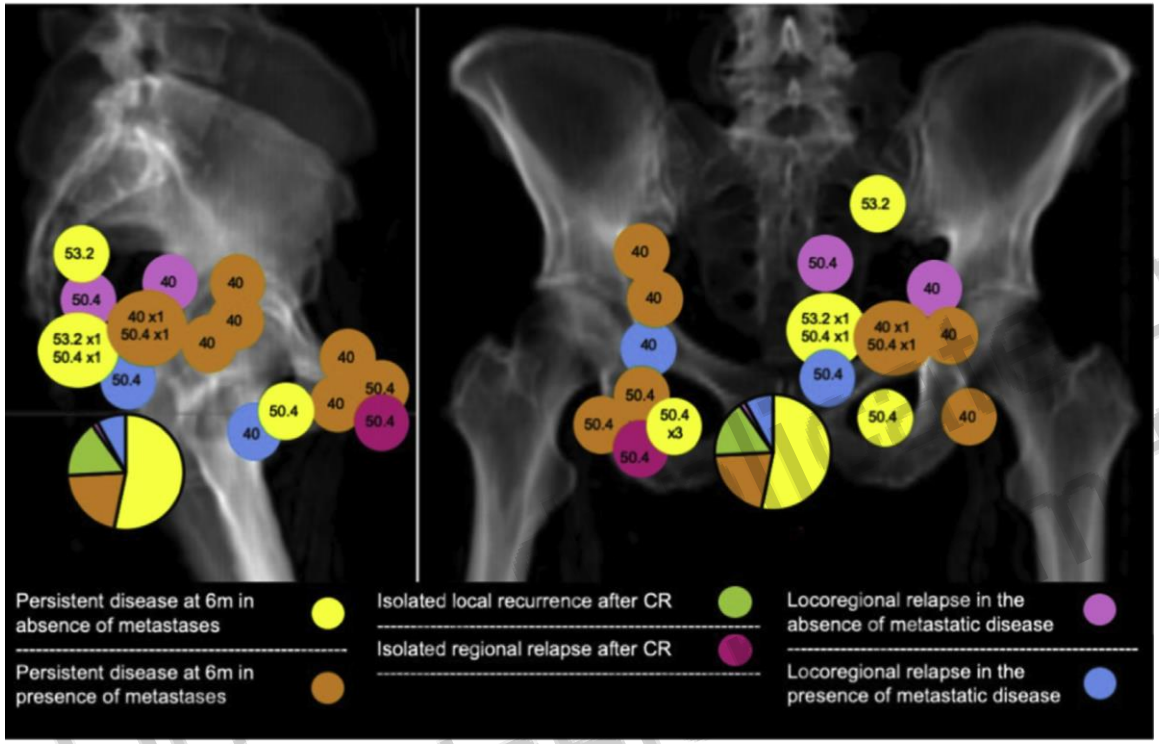
Planning and delivery:

Volumetric modulated arc therapy (VMAT), employing a dual-arc approach



Kachnich L et al; IJROBP 2013

IMRT in anal cancer: UK experience



- ✓T1-T2: 50.4 Gy/28 fr to primary tumor GTV
- ✓T3-T4 any N: 53.2 Gy/28 fr
- ✓N+ sized < 3 cm 50.4 Gy/28 fr
- ✓N+ sized > 3 cm 53.2 Gy/28 fr
- ✓Elective volumes (mesorectal, obturator, ext and int iliac, inguinal, presacral regions): 40 Gy/28 fr (biologically equivalent to 30.6 Gy/17 fr as per ACT II; α/β ratio= 8 Gy; loss 0.7 Gy after 20 fr)

- ✓ CR rate: 86.7%
- ✓ 3-year DFS: 75.6%
- ✓ 3-year OS: 85.6%
- ✓ All relapses: 83.4% at site of primary disease
- ✓ Only 2 isolated isolated relapses nodal regions (0.5%)

Shakir R et al – IJROBP 2020

Franco *et al. Radiation Oncology* (2018) 13:172
https://doi.org/10.1186/s13014-018-1124-9

Radiation Oncology

RESEARCH Open Access

Comparing simultaneous integrated boost vs sequential boost in anal cancer patients: results of a retrospective observational study

Pierfrancesco Franco[1*], Berardino De Bari[2], Francesca Arcadipane[1], Alexis Lepinoy[3], Manuela Ceccarelli[4], Gabriella Furfaro[1], Massimiliano Mistrangelo[5], Paola Cassoni[6], Martina Valgiusti[7], Alessandro Passardi[7], Andrea Casadei Gardini[7], Elisabetta Trino[1], Stefania Martini[1], Giuseppe Carlo Iorio[1], Andrea Evangelista[4], Umberto Ricardi[1] and Gilles Créhange[8]

- 190 pts
  - SeqB: 103
  - SIB: 87

Propensity score matching

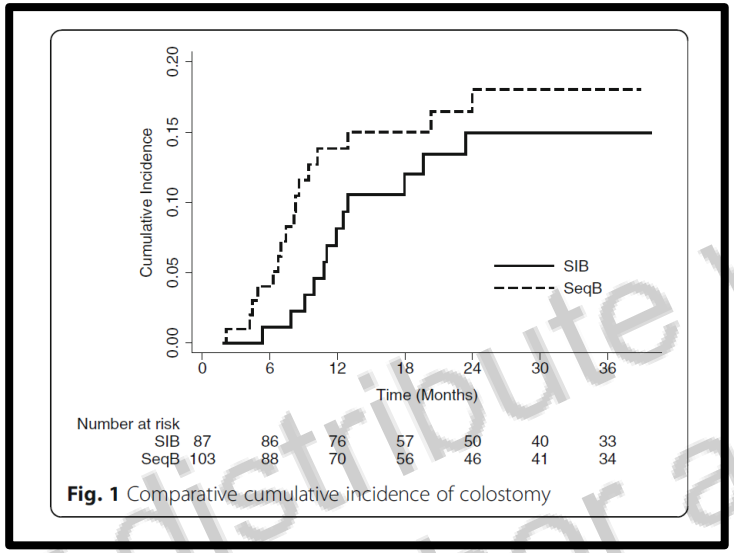


Fig. 1 Comparative cumulative incidence of colostomy

Comparative cumulative incidence of colostomies

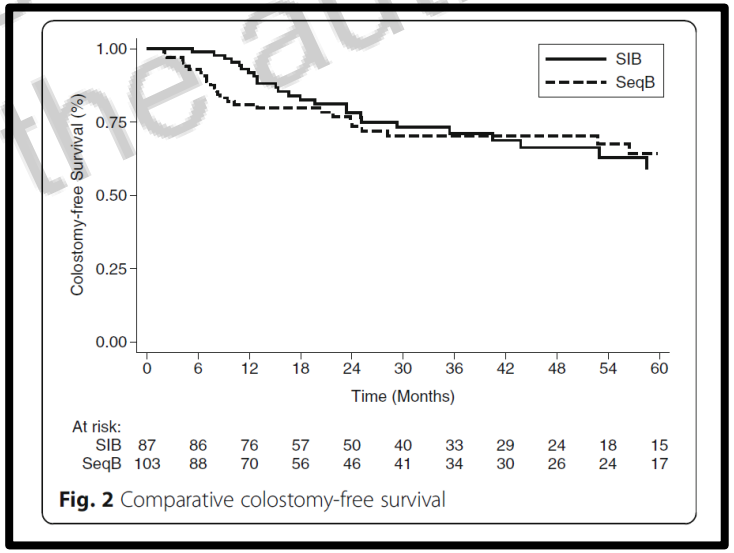


Fig. 2 Comparative colostomy-free survival

Comparative CFS

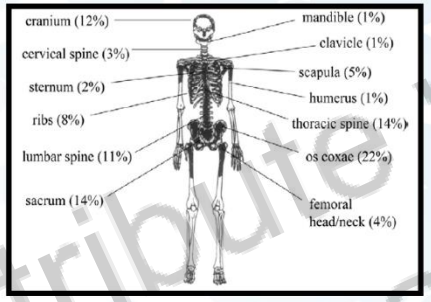
Franco et al et al – Radiat Oncol 2018

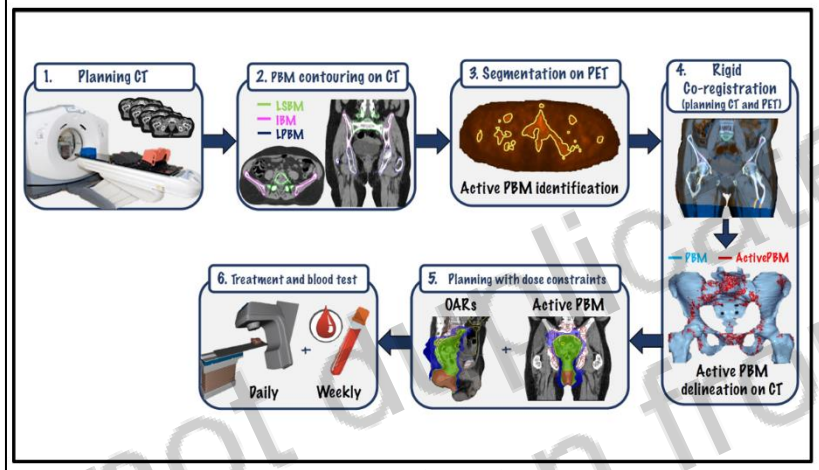
Bone marrow sparing IMRT to reduce acute hematologic toxicity in pts affected with SCC of the anal canal undergoing concurrent RT-CT: a phase II prospective trial

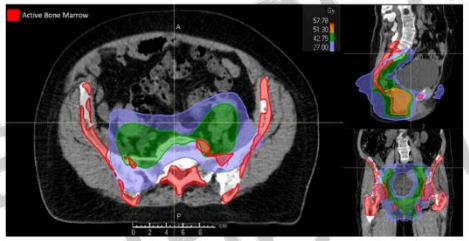
Hematologic toxicity: consequences
- Delayed CT cycles
- Missed CT cycles
- Hospitalization need (bleeding, infections, anemia)
- Growth factors need
- Limited room to further CT
- RT treatment breaks

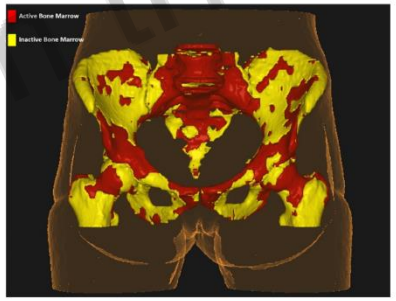
RTOG 98-11:
- G3-G4 HT: 61%
- Febrile neutropenia: 20%

RTOG 05-29:
- G3-G4 HT: 58%









- One-armed two-stage Simon's design
- Historical data of success (p0) represented by 42% G0-G2 HT within RTOG 05-29
- The threshold of successful trial (p1) for BM-sparing IMRT set to 62% of G0-G2 HT (G3-G4: 38%)
- α-error: 5% (one-sided type I error)
- β-error: 20% (type II error: power 80%)
- Step 1: 9/21 with G0-G2 HT; Step 1+ Step 2: 21/39 with G0-G2 HT

	LEUCOPENIA	NEUTROPENIA	ANEMIA	TROMBOCITOPENIA
1	G1	G0	G0	G0
2	G3	G4	G2	G0
3	G2	G0	G0	G0
4	G4	G4	G2	G2
5	G2	G2	G0	G0
6	G2	G1	G1	G0
7	G2	G0	G3	G0
8	G2	G2	G0	G0
9	G0	G0	G0	G0
10	G0	G0	G0	G0
11	G2	G2	G0	G0
12	G1	G0	G0	G1
13	G1	G0	G0	G0
14	G2	G2	G1	G1
15	G2	G1	G0	G0
16	G1	G0	G1	G0
17	G1	G2	G0	G0
18	G0	G0	G0	G0
19	G1	G1	G0	G0
20	G3	G3	G1	G2
21	G0	G0	G1	G0

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First International Multidisciplinary Anal Cancer Conference

Arcadipane et al; Cancers 2020
Arcadipane et al; J Pers Med 2021

VOLUME 28 · NUMBER 34 · DECEMBER 1 2010
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

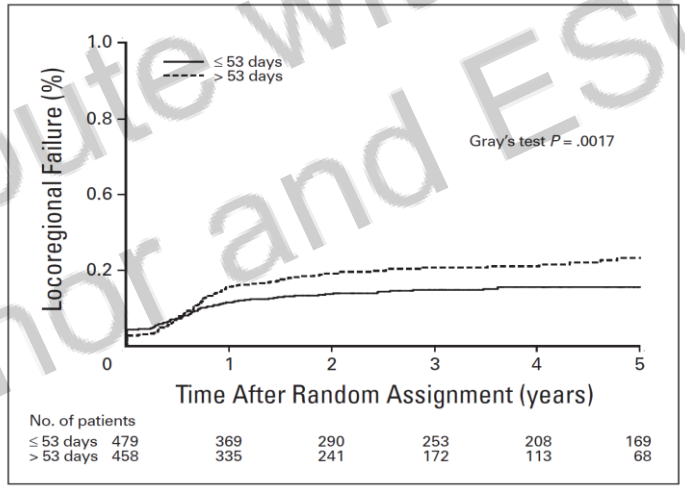
The impact of OTT on local control and survival in anal cancer: pooled data – RTOG 87-04 and RTOG 98-11

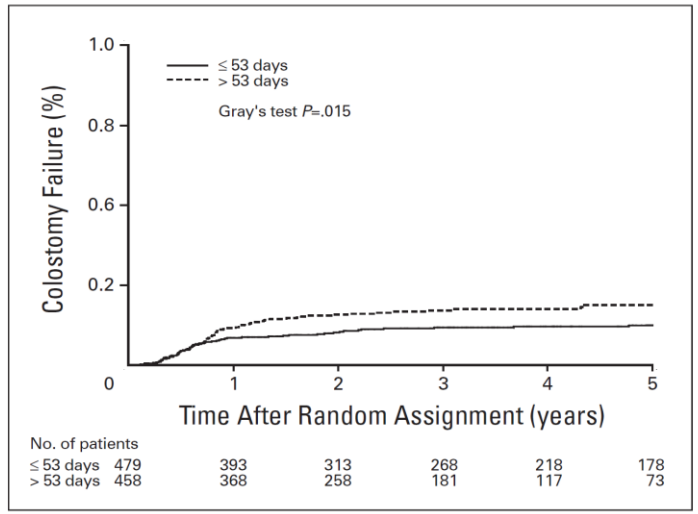
Impact of Overall Treatment Time on Survival and Local Control in Patients With Anal Cancer: A Pooled Data Analysis of Radiation Therapy Oncology Group Trials 87-04 and 98-11

Edgar Ben-Josef, Jennifer Moughan, Jaffer A. Ajani, Marshall Flam, Leonard Gunderson, JonDavid Pollock, Robert Myerson, Rani Anne, Seth A. Rosenthal, and Christopher Willett

	RT+5FU+MMC	RT+FU+CDDP	RT+5FU	Total
Factor	n=472	n=320	n=145	n=937
RT duration (days)				
Mean	45	45	39	44
Range	0-158	0-107	7-96	0-158
CT duration (days)				
Mean	31	87	31	32
Range	0-60	0-141	0-72	0-141
OTT (days)				
Mean	45	101	39	53
Range	1-158	0-163	7-96	0-163

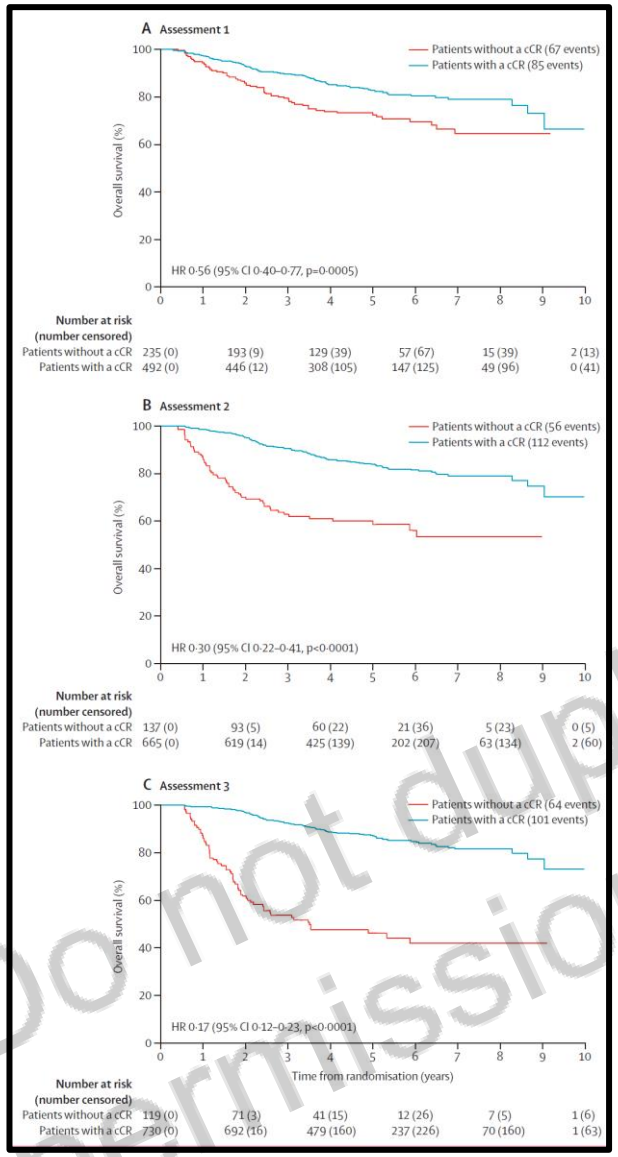
Higher colostomy and loco-regional failure if treatment time > 53 days





Ben Josef et al; JCO 2010

Time for response assessment



Articles

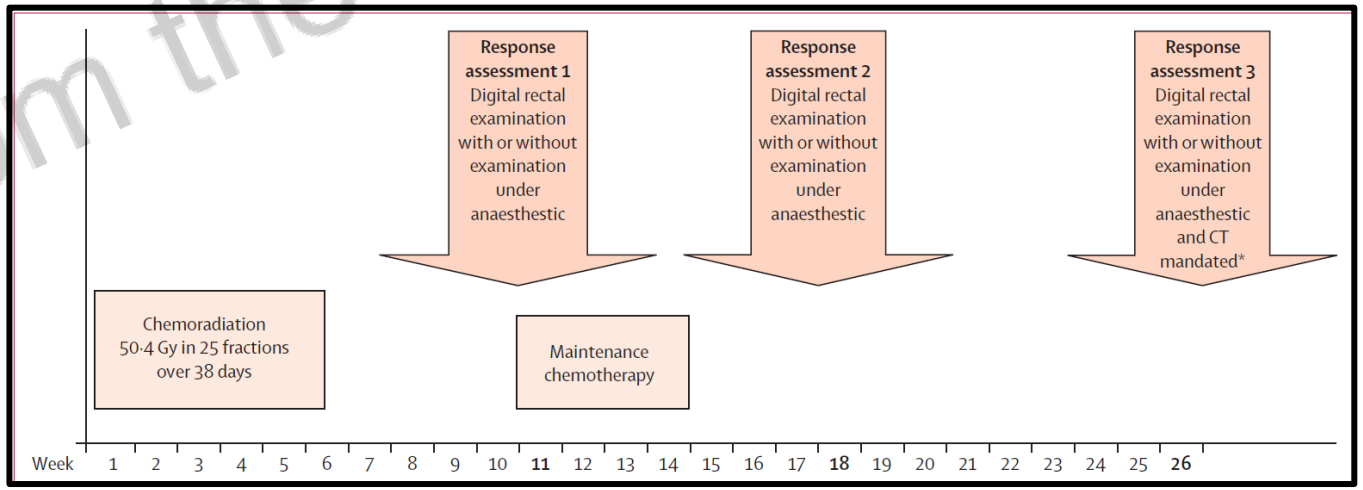
Best time to assess complete clinical response after chemoradiotherapy in squamous cell carcinoma of the anus (ACT II): a post-hoc analysis of randomised controlled phase 3 trial

Robert Glynne-Jones, David Sebag-Montefiore, Helen M Meadows, David Cunningham, Rubina Begum, Fawzi Adab, Kim Benstead, Robert J Harte, Jill Stewart, Sandy Beare, Allan Hackshaw, Latha Kadalayil, on behalf of the ACT II study group

	Patients with complete clinical response	Patients without complete clinical response	Patients with unknown response data*
Assessment 1	441	209	41
Assessment 2	556	106	29
Assessment 3†	590	88	13

*Patients classified as "unknown" attended the assessment but had response data that were inconclusive.
†23 patients died before assessment 3. Some patients did not attend for more than one assessment or had missing response data for more than one assessment so it is not possible to sum these numbers over all three timepoints.

Table 2: **Distribution of patients and tumour response for patients who attended all three assessments (n=691)**



Glynne-Jones et al –Lancet Oncol 2017

Articles

Nivolumab for previously treated unresectable metastatic anal cancer (NCI9673): a multicentre, single-arm, phase 2 study

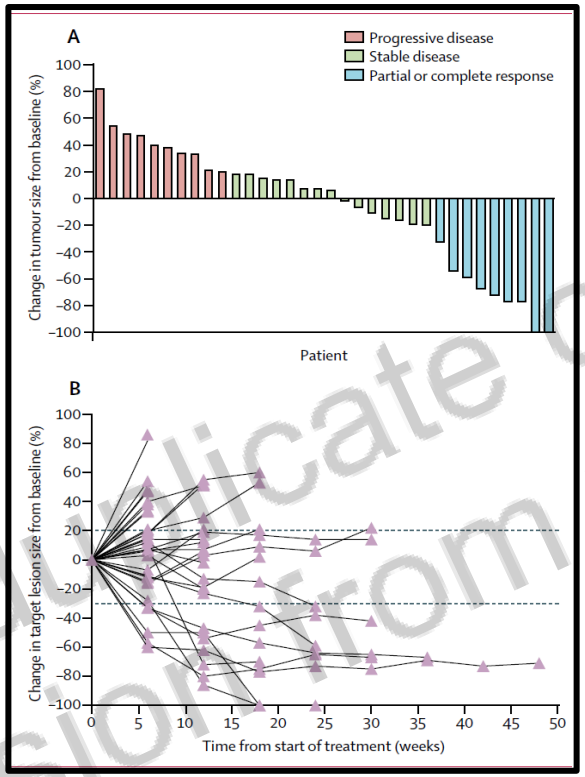
Van K Morris, Mohamed E Salem, Halla Nimeiri, Syma Iqbal, Preet Singh, Kristen Ciombor, Blase Polite, Dustin Deming, Emily Chan, James L Wade, Lianchun Xiao, Tanios Bekaii-Saab, Luis Vence, Jorge Blanda, Armeen Mahvash, Wai Chin Foo, Chimela Ohaji, Manolo Pasia, Gail Bland, Aki Ohinata, Jane Rogers, Amir Mehdizadeh, Kimberly Banks, Richard Lanman, Robert A Wolff, Howard Streicher, James Allison, Padmanee Sharma, Cathy Eng

Nivolumab every 2 weeks (3 mg/kg)
Primary end-point: response (RECIST v1.1), ITT
9/37 responses (24%); CR: 2/37 (5%); PR: 7/37 (19%)
Durable responders: 7/9 (78%)
Median duration of response: 5.8 months

	n=37
Median age (years)	56 (51–64)
Race	
White	33 (90%)
Black	2 (5%)
Asian	2 (5%)
Sex	
Male	10 (27%)
Female	27 (73%)
ECOG performance status	
0	10 (27%)
1	27 (73%)
HIV positive	2 (5%)
Median number of prior lines of therapy	2 (1–7)
Distribution of unresectable disease	
Local recurrence	15 (41%)
Distant metastasis	37 (100%)
Sites of distant metastases	
Lung	19 (51%)
Liver	14 (38%)
Lymph node	10 (27%)
Soft tissue	5 (14%)

Data are n (%) or median (IQR). ECOG=Eastern Cooperative Oncology Group.

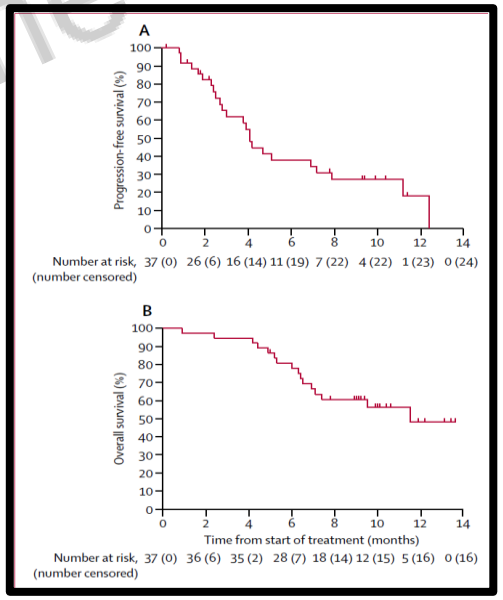
Table 1: **Baseline demographics**

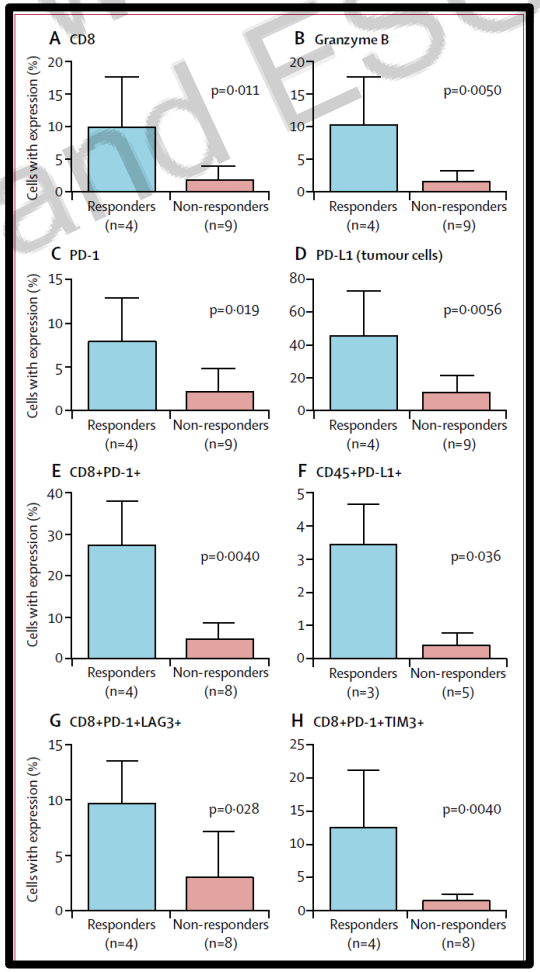


	Grade 1	Grade 2	Grade 3
Anaemia	13 (35%)	11 (30%)	2 (5%)
Fatigue	17 (46%)	7 (19%)	1 (3%)
Rash	8 (22%)	2 (5%)	1 (3%)
Constipation	8 (22%)	2 (5%)	0
Anorexia	5 (14%)	4 (11%)	0
Diarrhoea	8 (22%)	0	0
Weight loss	5 (14%)	1 (3%)	0
Arthralgia	3 (8%)	3 (8%)	0
Hyperglycaemia	3 (8%)	1 (3%)	0
Hypothyroidism	1 (3%)	1 (3%)	1 (3%)
Lymphoedema	1 (3%)	1 (3%)	0
Nausea	2 (5%)	0	0
Pneumonitis	0	1 (3%)	0

Data are n (%). n=37.

Table 2: **All adverse events**





Median PFS: 4.1 months
6-month PFS: 38%
Median OS: 11.5 months
Estimated 1-year OS: 48%

Morris et al et al – Lancet Oncol 2017

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 28: 1036–1041, 2017
doi:10.1093/annonc/mdx029
Published online 7 February 2017

ORIGINAL ARTICLE

Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with recurrent carcinoma of the anal canal

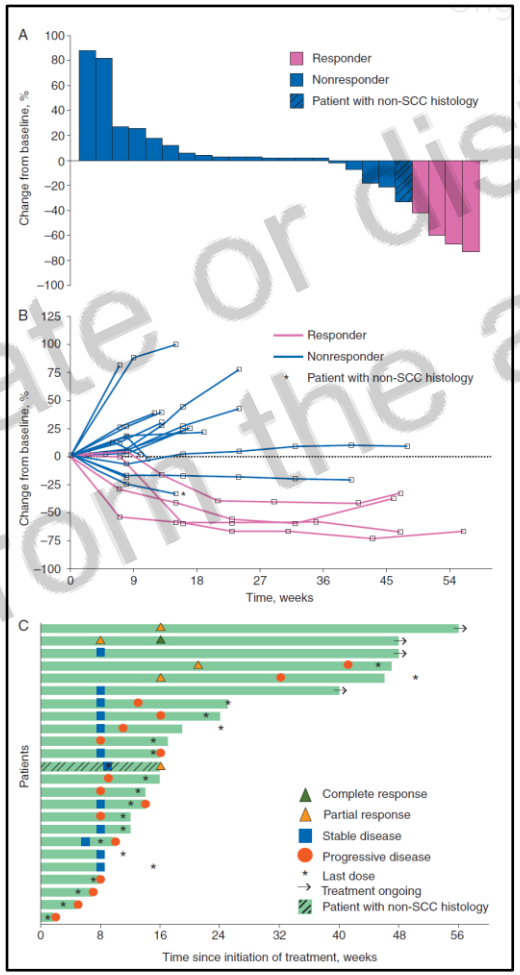
P. A. Ott[1*], S. A. Piha-Paul[2], P. Munster[3], M. J. Pishvaian[4], E. M. J. van Brummelen[5], R. B. Cohen[6], C. Gomez-Roca[7], S. Ejadi[8], M. Stein[9], E. Chan[10], M. Simonelli[11], A. Morosky[12], S. Saraf[12], K. Emancipator[12], M. Koshiji[12] & J. Bennouna[13]

Pembrolizumab every 2 weeks (10 mg/kg) for up to 2 year or PD or unacceptable toxicity
PD-L1 ≥1% +ve tumors
Primary end-point: safety and overall response rate (RECIST v 1.1)
Secondary end-points: PFS, OS, response duration

Table 2. Treatment-related adverse events

Any-grade adverse events occurring in ≥ 2 patients, *n* (%)	***N* = 25**
Diarrhea	4 (16)
Fatigue	4 (16)
Nausea	3 (12)
Dry mouth	2 (8)
Hypersensitivity	2 (8)
Hypothyroidism	2 (8)
Night sweats	2 (8)
Stomatitis	2 (8)
Thrombocytopenia	2 (8)
Vomiting	2 (8)
Grade 3–4 adverse events occurring in ≥ 1 patient, *n* (%)	
Colitis (grade 3)[a]	1 (4)
Diarrhea (grade 3)[a]	1 (4)
General physical health deterioration (grade 3)	1 (4)
Increased blood thyroid stimulating hormone (grade 3)	1 (4)

[a]Occurred in the same patient.

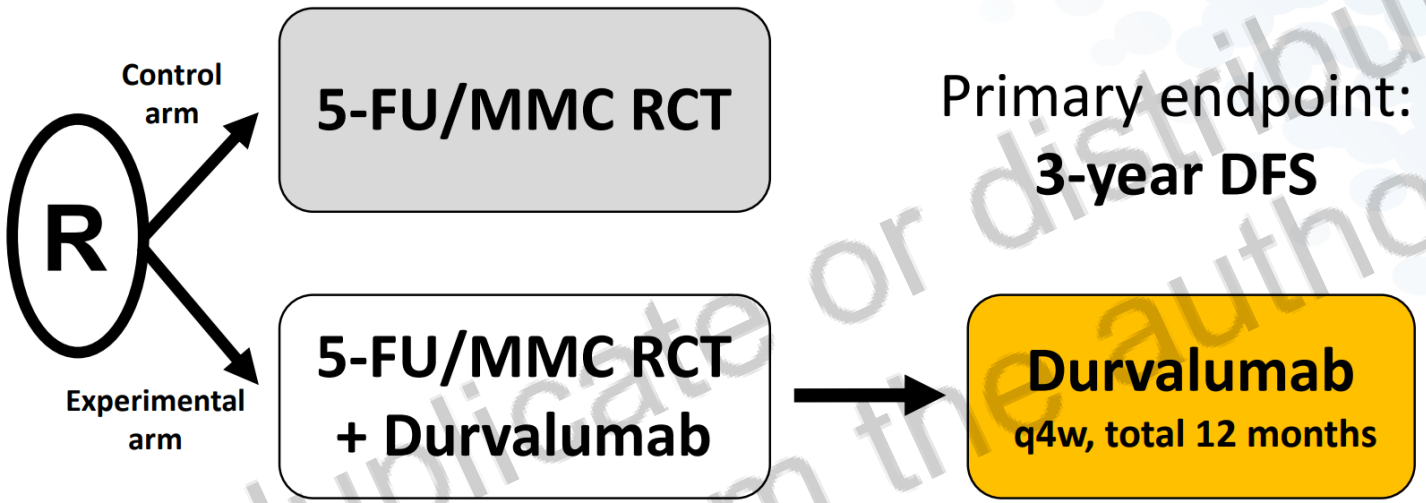


- ✓ PD-L1 ≥1: 32 pts (74%); enrolled 25 and 24 analysed
- ✓ Overall response rate: PR: 4/24 (17%); SD 10/24 (42%)
- ✓ Disease control: 14/24 (58%)
- ✓ 2/4 responders: duration of response > 9 months
- ✓ Median PFS: 3 months
- ✓ 6-month PFS: 31.6%
- ✓ 12-month PFS: 19.7%
- ✓ Median OS: 9.3 months
- ✓ 6-month OS: 64.5%
- ✓ 12-month OS: 47.6%

Otti et al – Ann Oncol 2017

IMACC Visual Abstract

RADIANCE - Radiochemotherapy +/- Durvalumab in locally-advanced anal cancer: A randomized multicenter phase II trial



Primary endpoint:
3-year DFS

Recruitment to date: n=31 of 178 pts

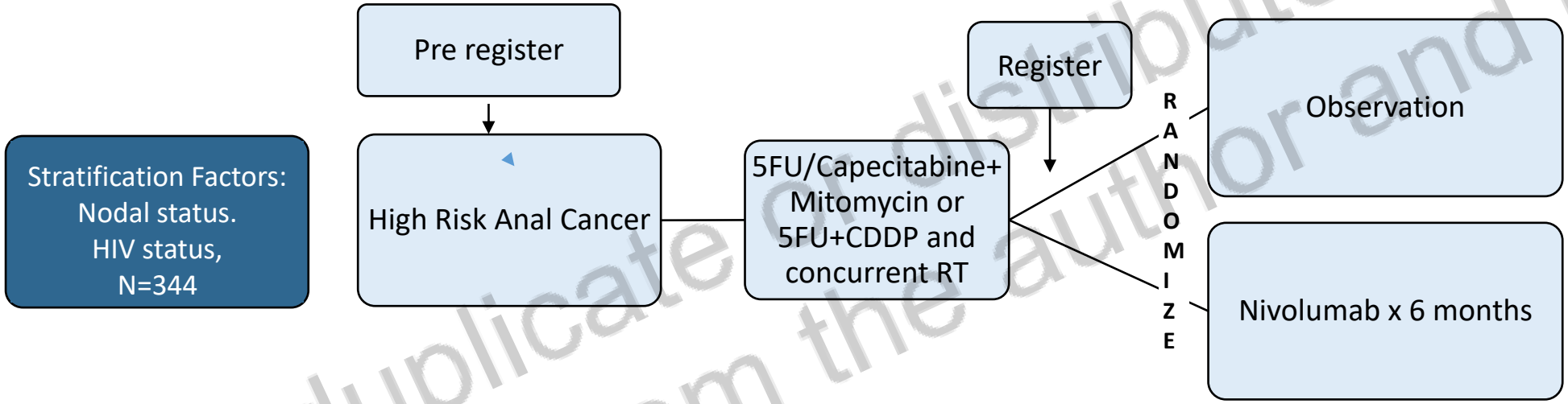
- **T2 ≥4cm, T3-4 and/or cN+ anal carcinoma; Durvalumab (PD-L1 ICI) start 2 weeks before RCT**
- **Hypothesis: Durvalumab will improve the 3-year DFS from 60% in the control arm to 80% in the experimental arm**
- **23 centers; PI: Emmanouil Fokas; NCT04230759; Homepage: www.radiance-studie.de**

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

Balermpas et al, Oncoimmunol 2017*
Martin et al. BBA-Rev Cancer 2017
Martin et al. Front Immunol 2017
Martin et al. Cancer Treat Rev 2018
Martin et al. Strahlen Onkol 2019
Martin et al. CTRO 2020

Courtesy Emanuel Fokas @IMACC2020 webinar

EA2165: Randomised Phase II Trial OF Nivolumab Following Chemoradiotherapy CI Rajdev

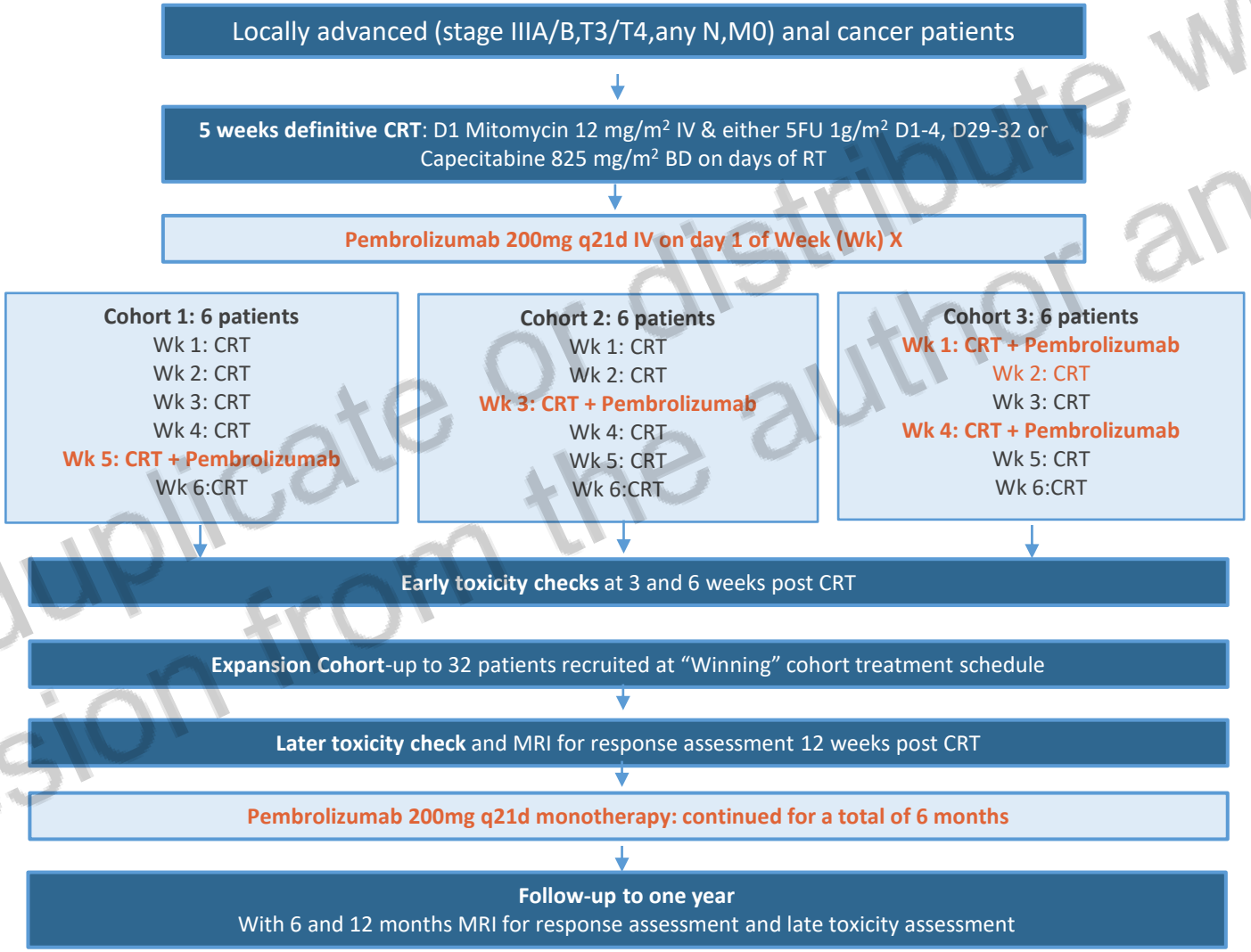


PI: L. Rajdev

stage II (T3N0 only), IIIA, or IIIB invasive anal (anal margin) squamous cell carcinoma 54Gy

Primary endpoint: 2-yr DFS (Goal of 62.5% vs. 45%)
Secondary endpoints: CFS, OS, Toxicityity

CORINTH Trial CI Hall

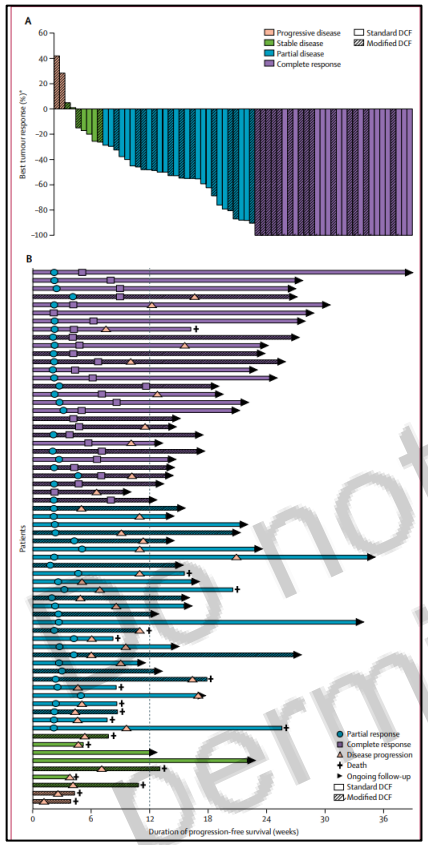


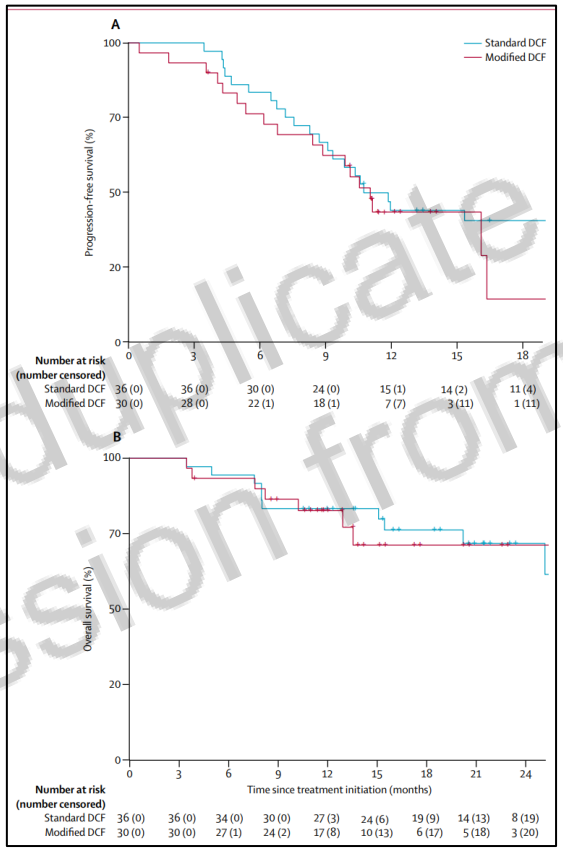
Articles

Docetaxel, cisplatin, and fluorouracil chemotherapy for metastatic or unresectable locally recurrent anal squamous cell carcinoma (Epitopes-HPV02): a multicentre, single-arm, phase 2 study

Stefano Kim, Eric François, Thierry André, Emmanuelle Samalin, Marine Jary, Farid El Hajbi, Nabil Baba-Hamed, Simon Pernot, Marie-Christine Kaminsky, Olivier Bouché, Jérôme Desrame, Mustapha Zoubir, François Ghiringhelli, Aurélie Parzy, Christelle De La Fouchardiere, Denis Smith, Mélanie Deberne, Laurie Spehner, Nicolas Badet, Olivier Adotevi, Amélie Anota, Aurélia Meurisse, Devi Vernerey, Julien Taieb, Véronique Vendrely, Bruno Buecher, Christophe Borg

modified DCF (40 mg/m² docetaxel and 40 mg/m² cisplatin on day 1 and 1200 mg/m² per day of fluorouracil for 2 days, every 2 weeks) x 8 cycles





original reports

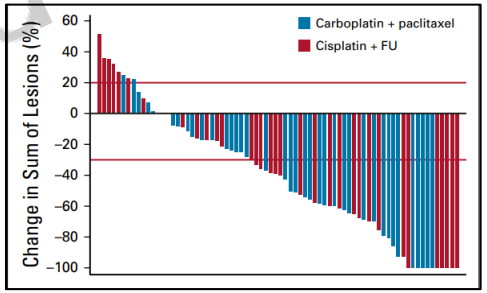
International Rare Cancers Initiative Multicent… Randomized Phase II Trial of Cisplatin and Fluorouracil Versus Carboplatin and Paclitaxel in Advanced Anal Cancer: InterAAct

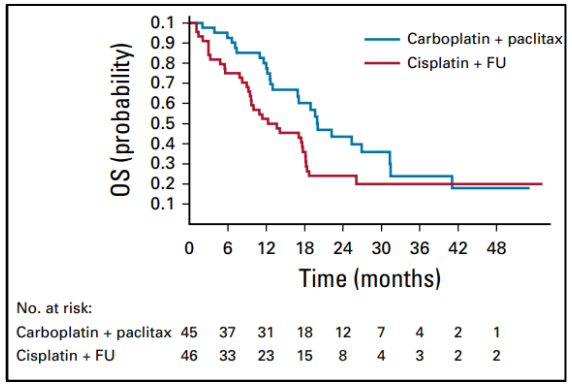
Sheela Rao, MD[1]; Francesco Sclafani, MD, PhD[1]; Cathy Eng, MD[2]; Richard A. Adams, MD[3]; Marianne G. Guren, MD, PhD[4]; David Sebag-Montefiore, MD[5]; Al Benson, MD[6]; Annette Bryant[1]; Clare Peckitt, MSc[1]; Eva Segelov, PhD[7]; Amitesh Roy, MSc, MD[8]; Matt T. Seymour, MA, MD[5]; Jack Welch, MD, PhD[9]; Mark P. Saunders, PhD[10]; Rebecca Muirhead, MD[11]; Peter O'Dwyer, MD[12]; John Bridgewater, PhD[13]; Shree Bhide, MRCP, PhD[14]; Rob Glynne-Jones, MD[15]; Dirk Arnold, MD[16]; and David Cunningham, MD FRCP[1]

TABLE 2. Summary of Objective Response

Response (RECIST 1.1)	Carboplatin Plus Paclitaxel (n = 39) No.	%	Cisplatin Plus FU (n = 35) No.	%
CR	5	12.8	6	17.1
PR	18	46.2	14	40
SD	10	25.6	7	20.0
PD	6	15.4	8	22.9
CR/PR	23	59	20	57.1
95% CI	42.1 to 74.4		39.4 to 73.7	

Abbreviations: CR, complete response; FU, fluorouracil; PD, progressive disease; PR, partial response; SD, stable disease.





Kim S, et al; Lancet Oncol 2018
Rao S, e tal; JCO 2020

IMACC Visual Abstract

A Phase III Randomized Nordic Anal Cancer Group Study on Circulating Tumor DNA (pHPV) guided Follow-Up

SCCA → CRT → P16/HPV positive → ®

- A: SOC-FU → Biobanking every 3-4 months → Disease-free survival at two years FU
- B: SOC- cfDNA guided -FU → ctDNA analyses
  - Positive → PET-CT → Early intervention
  - Negative → SOC → B: SOC- cfDNA guided -FU

Intervention:
plasma HPV guided follow-up

Primary endpoint:
Disease free survival at 2 years

Sample size:
N = 400

Inclusion criteria:
- **Patients with SCCA eligible for definitive CRT**
- **≥ 18 of years**
- **Written and oral consent**

- **HPV negative patients will be included, and followed similar to ARM A, with SOC + biobank**
- **Samples will be shipped and analyzed in central laboratory, or after QA in local labs.**

Trial Management group;

Karen-Lise Garm Spindler, DK, PI
Marianne Guren, NO
Anders Johnsson, SE
Pia Østerlund, FI
Laboratory Lead, Niels Pallisgard, DK

External review board;
Olav Dahl No, Bengt Glimelius, SE,
and Anders Jakobsen,DK

NOAC

Karen-Lise Garm Spindler, *MD, PhD, DMSc*

Department of Experimental Clinical Oncology
Aarhus University Hospital, Aarhus University
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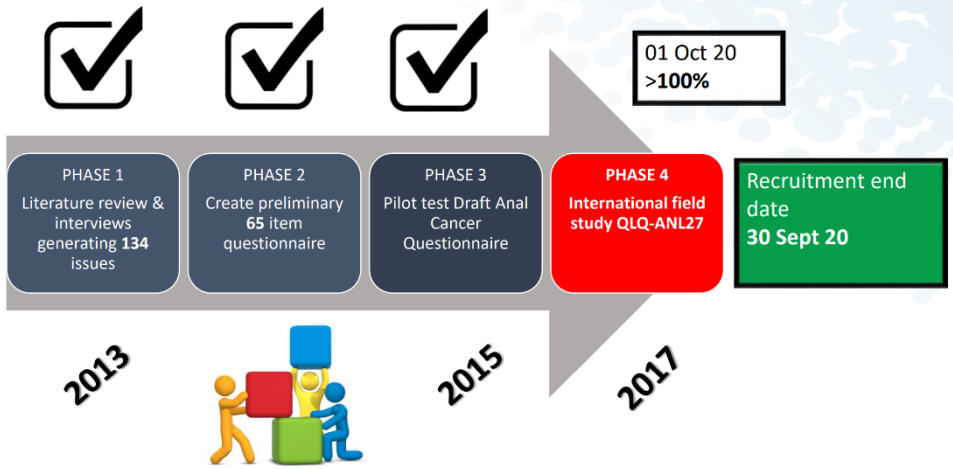
First International Multidisciplinary Anal Cancer Conference

Courtesy Karen-Lise Garm Spindler @IMACC2020 webinar

EORTC QLG Module Development



ANL27 module

- **EORTC QLQ-ANL27**
  - 27 questions
  - **4** hypothesised subscales
    - **Bowel function** (5 items)
    - **Pain** or discomfort (6 items)
    - **Stoma**-related (3 items)
    - **Sexual** function (7 items and 1 screening question)
  - **5** single questions

Phase IV: International Validation

- **Identify Psychometric properties of the EORTC QLQ-ANL27**
  - Scale structure
  - Reliability: Internal; Test-Retest high (n=25) and low symptom presentation (n=25)
  - Responsiveness to change (RCA): Improvement n=50; Deterioration n=50
  - Validity
  - Cross-cultural acceptability
- **Target sample size 375**
  - **Acute** n=125 (up to 3 months since treatment started)
  - **Early** n=125 (3 months – 1 year post-treatment)
  - **Late** n=125 (1-5 years post-treatment)

Courtesy Vasilis Vasiliou @IMACC2020 webinar

IMACC

First International Multidisciplinary Anal Cancer Conference

The Event | Tentative program | Registration | Venue | Abstracts | Abstract submission | Webinar May 6 | IMACC Faculty

The First International Multidisciplinary Anal Cancer Conference

Aarhus, Denmark. November 11-12, 2021

https://events.au.dk/imacc2021

Daniele Galliano – Senza titolo 2013

e-ESO – Live session 17.06.2021

Updates in the diagnosis and treatment of anal cancer

Pierfrancesco Franco MD, PhD
Dipartimento di Medicina Traslazionale, Università del Piemonte Orientale, Novara
Dipartimento di Radioterapia Oncologica, AOU 'Maggiore della Carità', Novara