Evolution des pratiques dans les cancers gynécologiques

30 novembre 2021

Hôtel Mercure Chartrons

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RADIOTHÉRAPIE - QUOI DE NEUF ?

ACTUALITÉS DES CONGRÈS SFRO ET ASTRO 2021

CANCER DE L'ENDOMETRE

Evolution des facteurs clinico-pathologiques « classiques »

GRADE

Importante variabilité inter-observateur

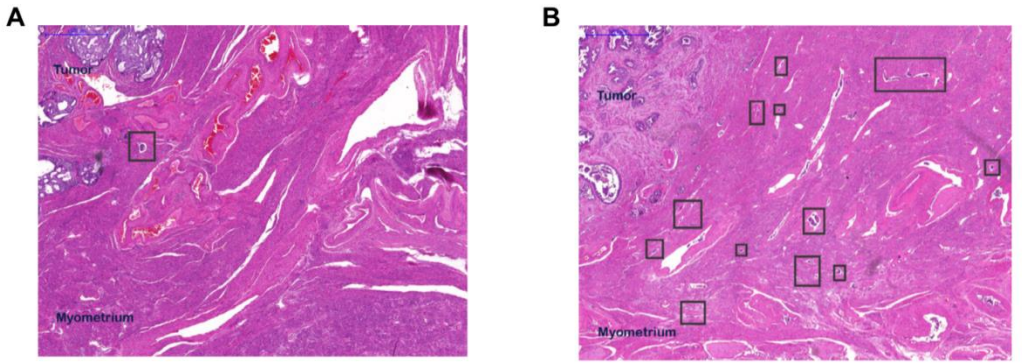
Le classement binaire du grade est recommandé :

- **carcinomes de grade 1 et 2 = carcinomes de bas grade**
- carcinomes de grade 3 comme = carcinomes de haut grade

Radiothérapie - Quoi de neuf ? (2021)

EMBOLS

Embols « substantiels » = agencement multifocal ou diffus d'embols ou présence de cellules tumorales **dans 5 espaces lymphovasculaire ou plus**



Facteur pronostique indépendant

- de la récidive pelvienne (HR 6.19, p<0.001),
- des métastases à distance (HR 3.61, p<0.001)
- de la survie globale (HR 2.02, p=0.002)

European Journal of Cancer (2015) 51, 1742– 1750

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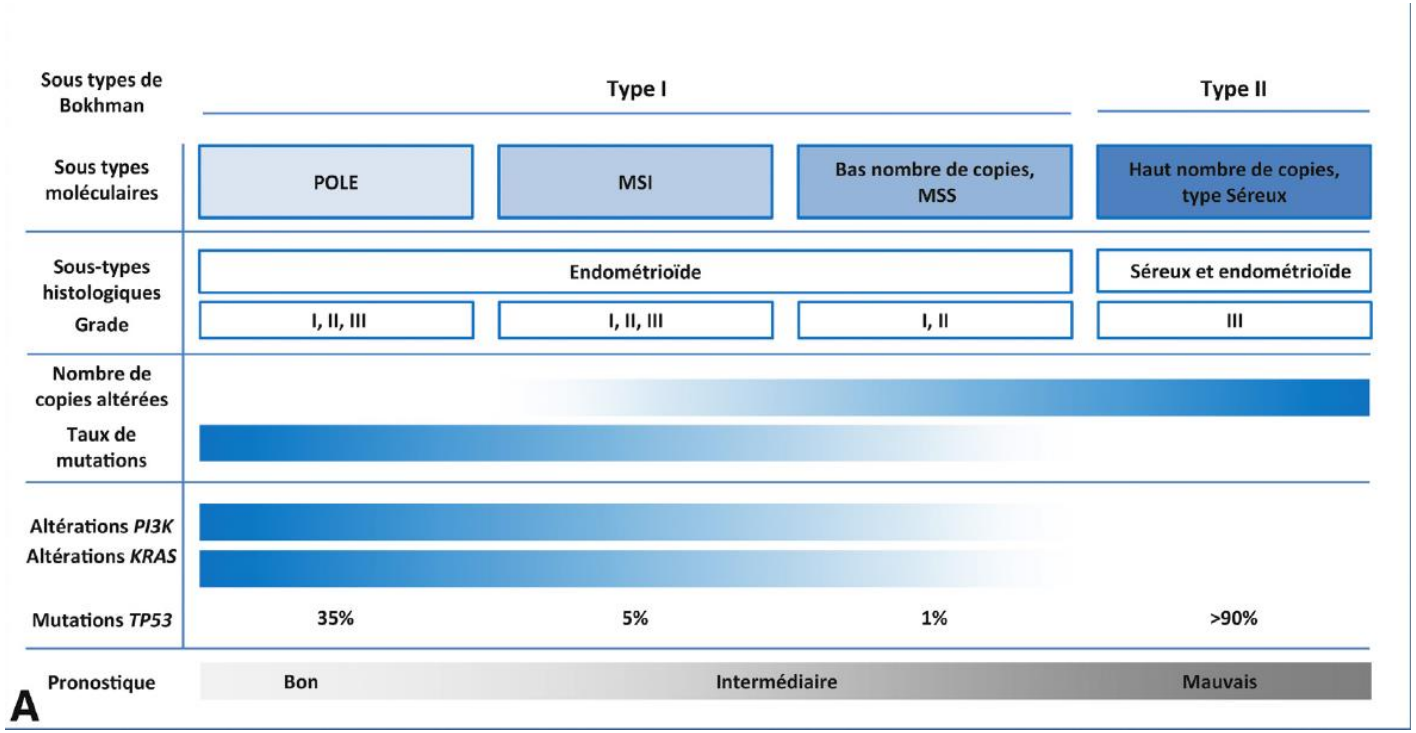
Classification moléculaire

- **La valeur pronostique de la classification binaire (type 1/ type 2) reste sous-optimale:**
  - 20 % des CE de type I rechutent
  - 15–20 % des CE type I sont en fait de haut grade
  - 50 % des CE de type II ne rechutent pas

- **TCGA*: 4 sous-types moléculaires pour les types cancers endométrioïdes et séreux**



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*The Cancer Genome Atlas Research Network. Nature,2013

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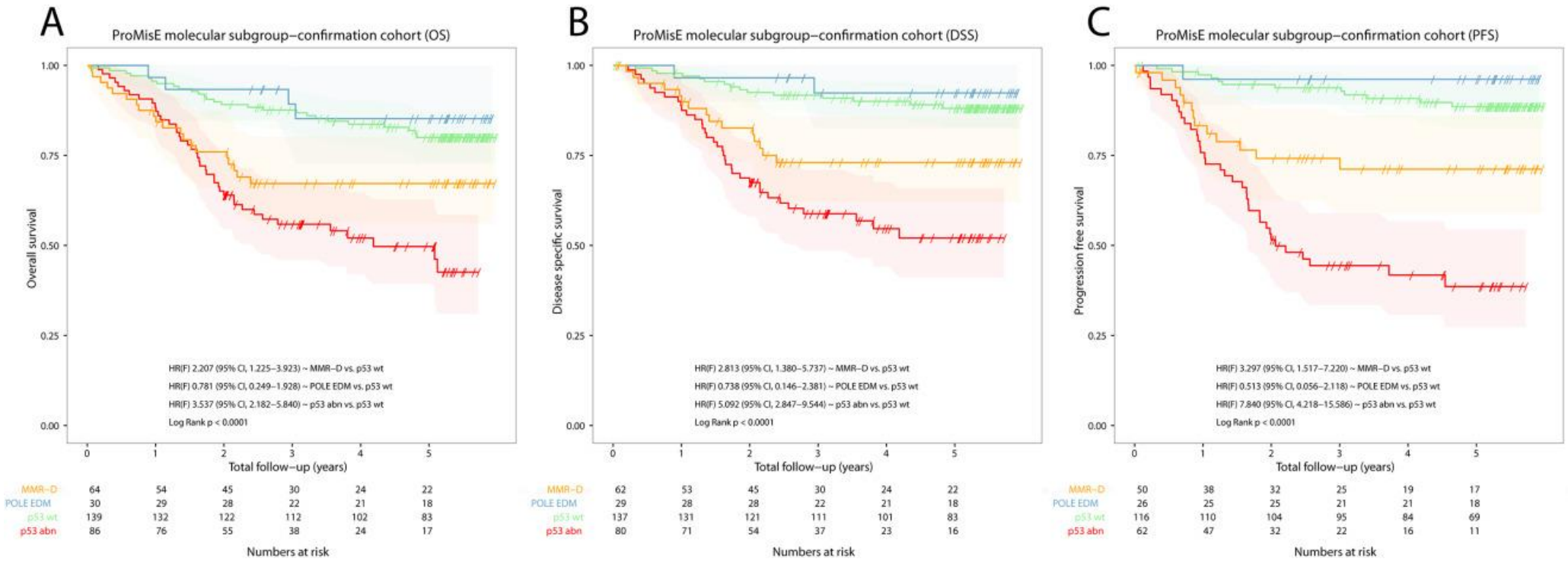
Classification moléculaire: quelle valeur pronostique ?

Confirmation of ProMisE: A simple, genomics-based clinical classifier for endometrial cancer



Radiothérapie - Quoi de neuf ? (2021)

Cancer 2017 , Volume: 123, Issue: 5, Pages: 802-813

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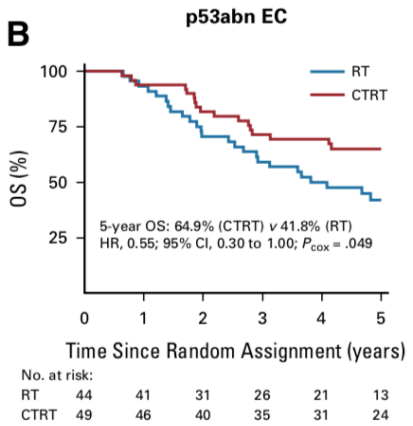
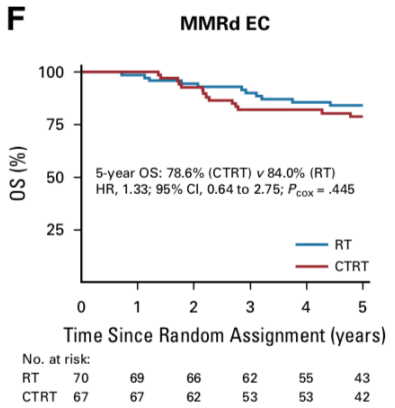
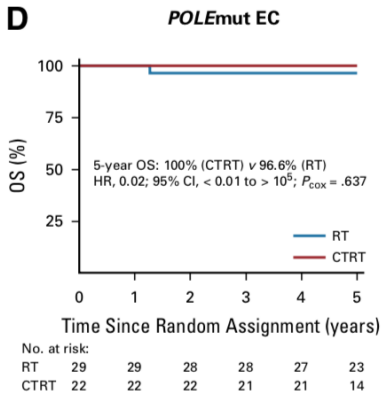
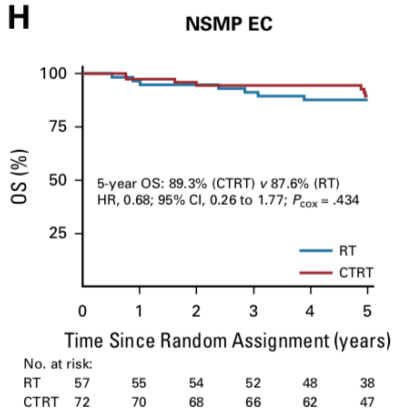
Classification moléculaire: quelle utilité clinique ?









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Molecular Classification of the PORTEC-3 Trial for High-Risk Endometrial Cancer: Impact on Prognosis and Benefit From Adjuvant Therapy

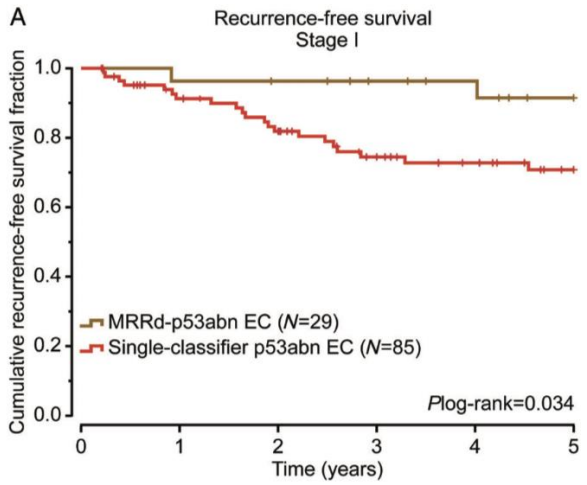
Alicia León-Castillo, MD[1]; Stephanie M. de Boer, MD[2]; Melanie E. Powell, MD[3]; Linda R. Mileshkin, MBBS[4]; Helen J. Mackay, MD[5]; Alexandra Leary, MD, PhD[6]; Hans W. Nijman, MD, PhD[6,7]; Naveena Singh, MD, MBBS[8]; Pamela M. Pollock, PhD[9]; Paul Bessette, MD[10]; Anthony Fyles, MD[11]; Christine Haie-Meder, MD[12]; Vincent T. H. B. M. Smit, MD, PhD[1]; Richard J. Edmondson, MD[13]; Hein Putter, MD[14]; Henry C. Kitchener, MD[13]; Emma J. Crosbie, MD, PhD[13]; Marco de Bruyn, PhD[7]; Remi A. Nout, MD[2]; Nanda Horeweg, MD, PhD[2]; Carien L. Creutzberg, MD, PhD[2]; and Tjalling Bosse, MD, PhD[1] on behalf of the TransPORTEC consortium

Survie globale et DFS:
Seul le groupe p53abn bénéficie de l'association RT-CT

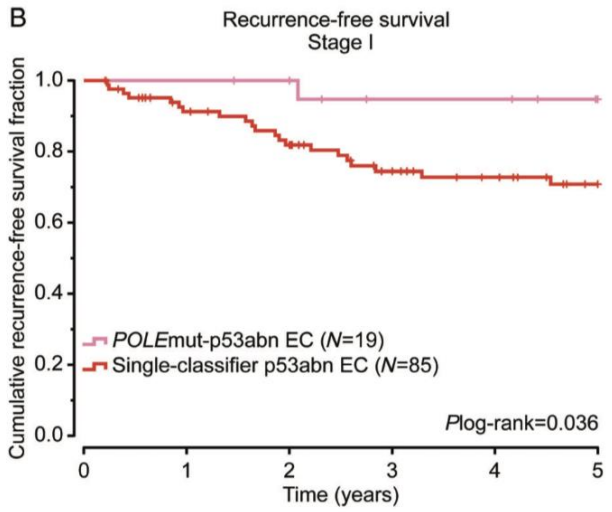
Alicia León-Castillo et al. J of Clinical Oncology 2020

CANCER DE L'ENDOMETRE

Comment prendre en charge les « multiple-classifier »?



MMRd ET p53 abn agrègent plutôt avec le groupe MMRd



POLEmut ET p53 abn agrègent avec le POLEmut

Radiothérapie - Quoi de neuf ? (2021)

Léon-Castillo et al. J Pathol 2020

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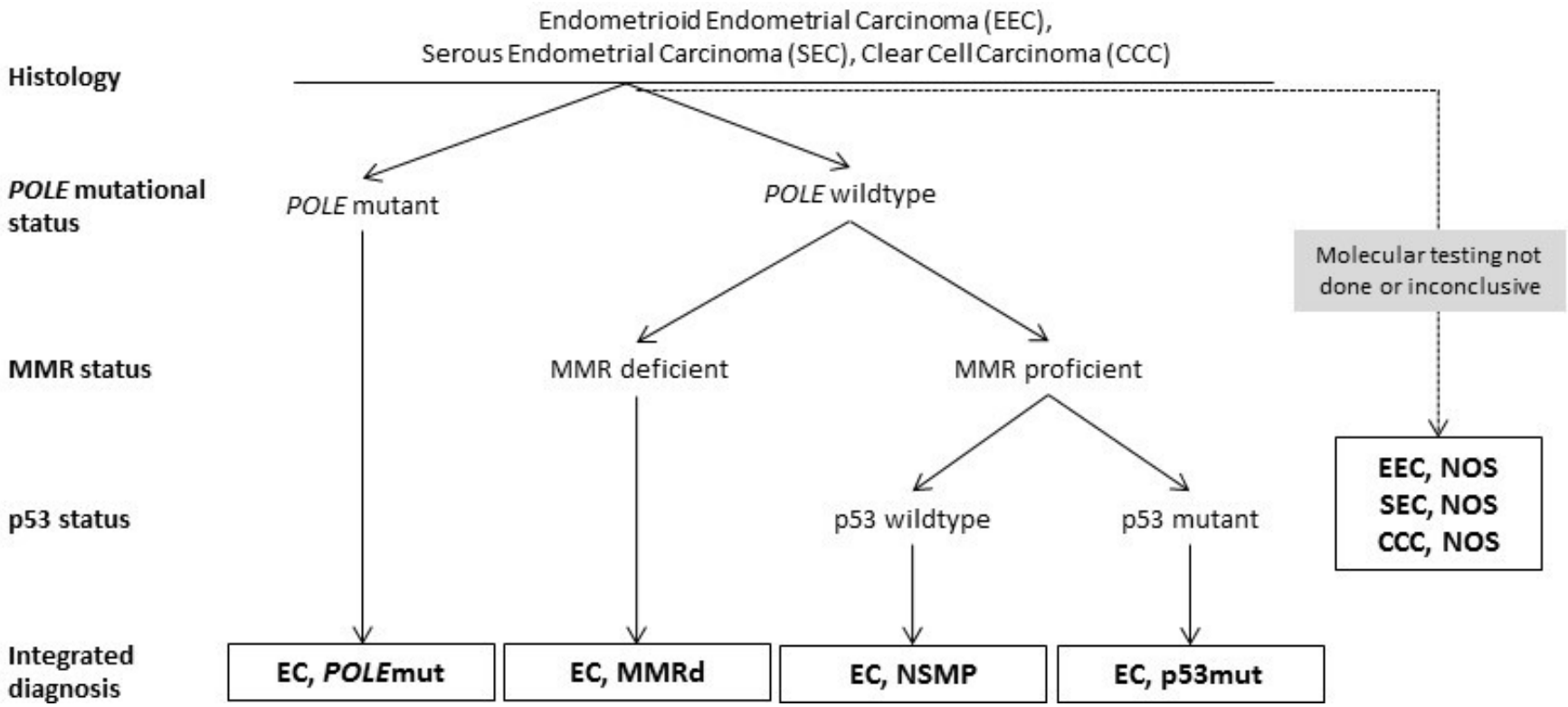
Classification moléculaire: en pratique ?



Radiothérapie - Quoi de neuf ? (2021)

van den Heerik ASVM, et al. Int J Gynecol Cancer 2020

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Recommandations ESGO-ESTRO-ESP 2020

ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma

Nicole Concin [1,2] Xavier Matias-Guiu,[3,4] Ignace Vergote,[5] David Cibula,[6] Mansoor Raza Mirza,[7] Simone Marnitz,[8] Jonathan Ledermann [9] Tjalling Bosse,[10] Cyrus Chargari,[11] Anna Fagotti,[12] Christina Fotopoulou [13] Antonio Gonzalez Martin,[14] Sigurd Lax,[15,16] Domenica Lorusso,[12] Christian Marth,[17] Philippe Morice,[18] Remi A Nout,[19] Dearbhaile O'Donnell,[20] Denis Querleu [12,21] Maria Rosaria Raspollini,[22] Jalid Sehouli,[23] Alina Sturdza,[24] Alexandra Taylor,[25] Anneke Westermann,[26] Pauline Wimberger,[27] Nicoletta Colombo,[28] François Planchamp,[29] Carien L Creutzberg[30]

Table 2 Definition of prognostic risk groups

Risk group	Molecular classification unknown	Molecular classification known*†

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Concin N et al. Int J Gynecol Cancer -2021

Table 2 Definition of prognostic risk groups

Risk group	Molecular classification unknown	Molecular classification known*†
Low	► Stage IA endometrioid + low-grade‡ + LVSI negative or focal	► Stage I–II ***POLEmut*** endometrial carcinoma, no residual disease ► Stage IA **MMRd/NSMP** endometrioid carcinoma + low-grade‡ + LVSI negative or focal
Intermediate	► Stage IB endometrioid + low-grade‡ + LVSI negative or focal ► Stage IA endometrioid + high-grade‡ + LVSI negative or focal ► Stage IA non-endometrioid (serous, clear cell, undifferentiared carcinoma, carcinosarcoma, mixed) without myometrial invasion	► Stage IB **MMRd/NSMP** endometrioid carcinoma + low-grade‡ + LVSI negative or focal ► Stage IA **MMRd/NSMP** endometrioid carcinoma + high-grade‡ + LVSI negative or focal ► Stage IA **p53abn** and/or non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) without myometrial invasion
High–intermediate	► Stage I endometrioid + substantial LVSI regardless of grade and depth of invasion ► Stage IB endometrioid high-grade‡ regardless of LVSI status ► Stage II	► Stage I **MMRd/NSMP** endometrioid carcinoma + substantial LVSI regardless of grade and depth of invasion ► Stage IB **MMRd/NSMP** endometrioid carcinoma high-grade‡ regardless of LVSI status ► Stage II **MMRd/NSMP** endometrioid carcinoma
High	► Stage III–IVA with no residual disease ► Stage I–IVA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) with myometrial invasion, and with no residual disease	► Stage III–IVA **MMRd/NSMP** endometrioid carcinoma with no residual disease ► Stage I–IVA **p53abn** endometrial carcinoma with myometrial invasion, with no residual disease ► Stage I–IVA **NSMP/MMRd** serous, undifferentiated carcinoma, carcinosarcoma with myometrial invasion, with no residual disease
Advanced metastatic	► Stage III–IVA with residual disease ► Stage IVB	► Stage III–IVA with residual disease of any molecular type ► Stage IVB of any molecular type

*For stage III–IVA *POLE*mut endometrial carcinoma and stage I–IVA MMRd or NSMP clear cell carcinoma with myometrial invasion, insufficient data are available to allocate these patients to a prognostic risk group in the molecular classification. Prospective registries are recommended.

†See text on how to assign double classifiers (eg, patients with both *POLE*mut and p53abn should be managed as *POLE*mut).

Pas de traitement adjuvant

Curiethérapie vaginale HDR
Option: surveillance, en particulier si patiente âgée de moins de 60 ans ou pour tumeurs intramuqueuses strictes

cN0: Radiothérapie
Curiethérapie seule si stade II, bas grade
pN0: Curiethérapie
Radiothérapie si embols ou stades II

Option: Chimiothérapie (haut grade, embols)

Radiothérapie externe et Chimiothérapie : concomitante et adjuvante ou traitement CT et EBRRT séquentiel
+/- **Boost en Curiethérapie** à considérer en cas d'embols nombreux, d'atteinte du stroma cervical, de stade IIIB/IIIC

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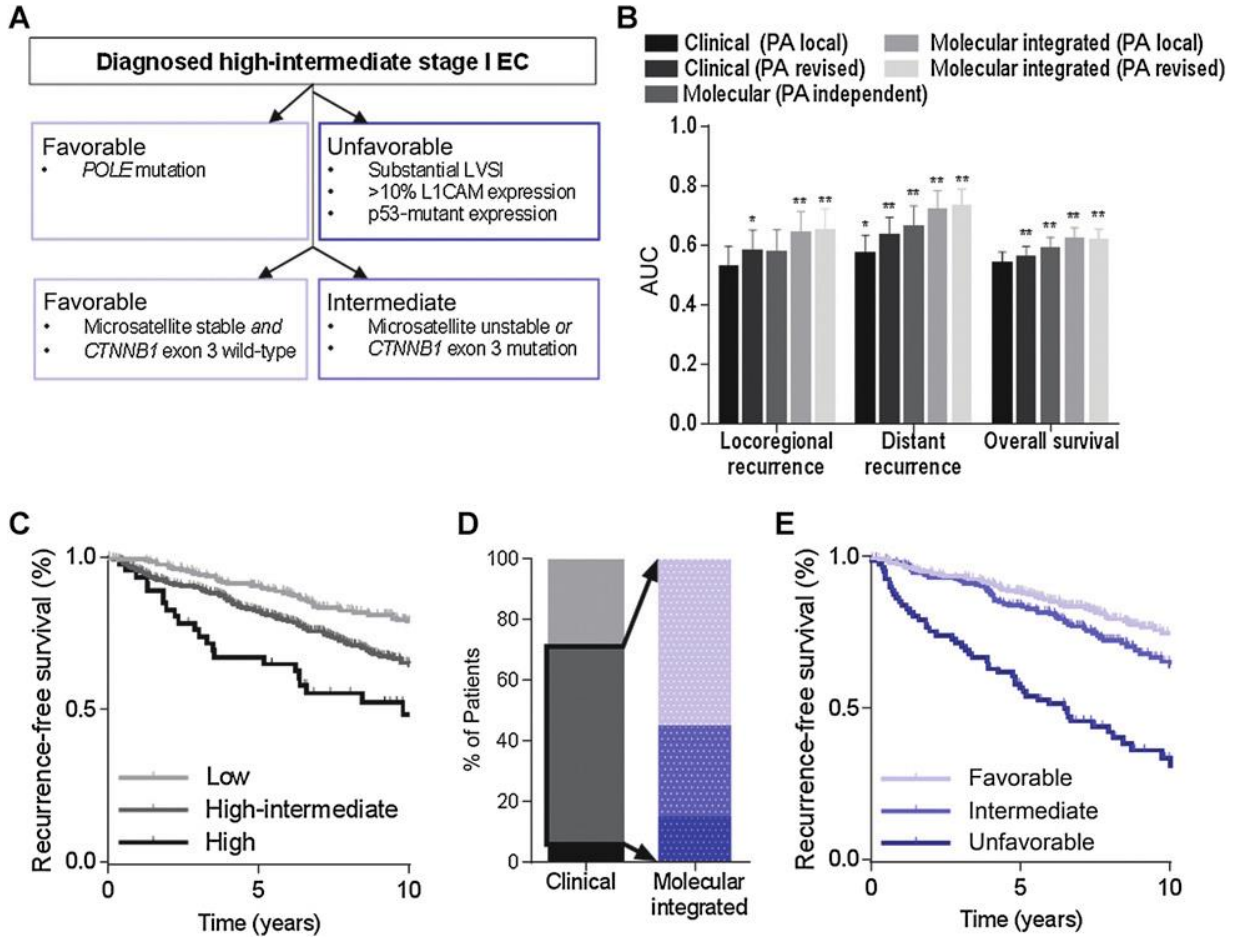
Vers un risque moléculaire intégré ?



Radiothérapie - Quoi de neuf ? (2021)

Stelloo Clin Cancer Research 2015

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EMBRACE 1

n= 1341
- ✓ IABT : 98% dosimétrie sur IRM
- ✓ OTT: 50 jours
- ✓ D90 CTV-HR: 87-90 Gy (EQD2)
- ✓ Chimiothérapie concomitante : 92%

FU : 51 mois

	Number of patients	CTV_{HR} volume, cm^{3}*	CTV_{HR} $D_{90\%}$ $EQD2_{10}$,Gy	Local failure (n)	Pelvic failure (n)	Any failure (n)	Patients dead (n)	5-year local control (95% CI)	5-year pelvic control (95% CI)	5-year disease-free survival (95% CI)	5-year overall survival (95% CI)
IB1	124	22 (17–27)	91 (87–95)	2	6	20	24	98% (94–100)	95% (87–98)	76% (67–83)	83% (75–89)
IB2	119	26 (20–38)	89 (84–93)	9	18	36	35	92% (84–96)	84% (75–90)	65% (56–73)	73% (64–81)
IIA1	38	23 (14–31)	91 (85–96)	3	4	6	7	91% (73–97)	88% (71–95)	75% (58–86)	80% (63–90)
IIA2	31	34 (24–42)	87 (80–91)	3	6	10	8	89% (68–96)	77% (55–89)	65% (44–79)	74% (53–87)
IIB	693	27 (19–36)	90 (86–95)	55	78	146	152	91% (88–93)	88% (85–90)	73% (69–76)	78% (75–82)
IIIA	13	30 (24–35)	84 (82–88)	0	0	2	3	100%	100%	76% (43–92)	76% (42–91)
IIIB	190	40 (30–56)	88 (83–91)	15	24	61	78	92% (86–95)	86% (79–90)	59% (52–66)	64% (57–71)
IVA	34	57 (39–89)	86 (78–89)	3	6	10	17	91% (75–97)	81% (62–91)	47% (28–63)	52% (33–68)
IVB	98	34 (22–47)	89 (85–92)	8	16	40	38	89% (79–95)	81% (70–88)	48% (37–58)	61% (49–70)
Total	1341†	28 (20–40)	90 (85–94)	98	158	331	363†	92% (90–93)	87% (85–89)	68% (65–70)	74% (72–77)

Data are n, median (IQR), or Kaplan-Meier estimates (95% CI). *Mean dose delivered over all fractions. †One patient with unknown FIGO stage. FIGO=The International Federation of Gynaecology and Obstetrics. CTV_{HR}= high-risk clinical target volume. $D_{90\%}$=minimal dose to 90% of the clinical target volume. $EQD2_{10}$=equi-effective dose in 2 Gy per fraction of 10 Gy.

Table 3:CTV_{HR} volume, and dose and clinical outcomes according to $FIGO_{2009}$ stage

Morbidité G ≥3:
- GU: 6.8% (95% CI 5.4-8.6)
- GI: 8.5% (6.9-10.6)
- Vaginale: 5.7% (4.3-7.6)
- Fistule: 3.2% (2.2-4.5)

Radiothérapie - Quoi de neuf ? (2021)

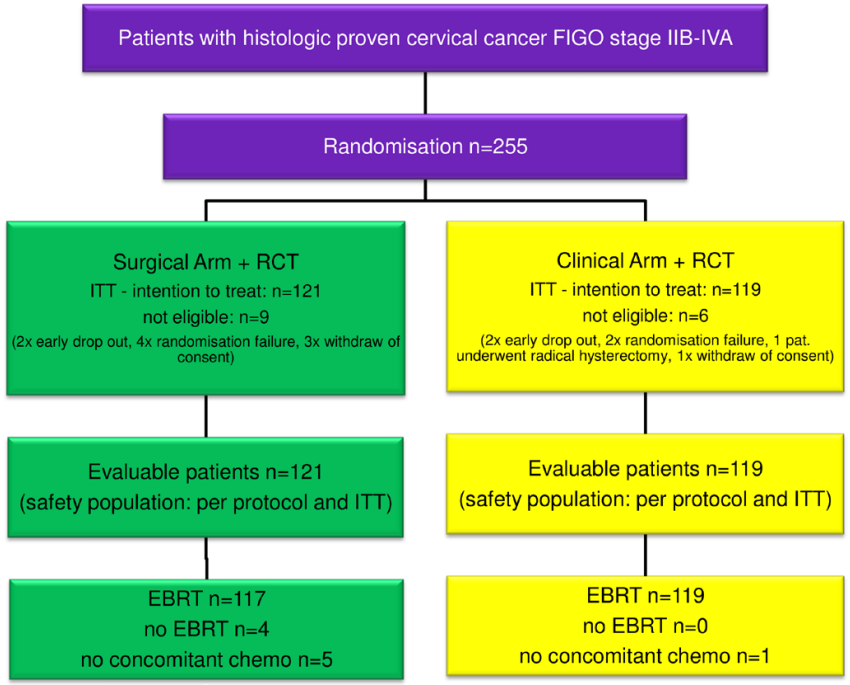
Pötter et al. Lancet Oncol 2021

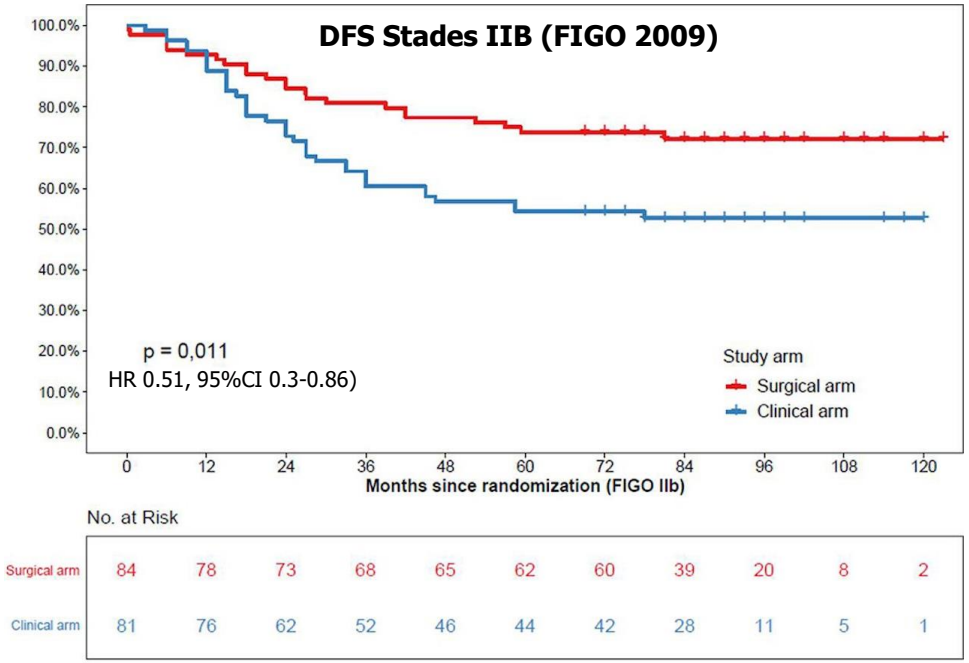
CANCER DU COL: LYMPHADENECTOMIE ?

UTERUS 11

Pas de différence de DFS (95%CI 0.48-1.05) p=0.084, sauf pour les stades IIB

Upstaging : 33% dans le bras lymphadénectomie
Champs étendus: 23% (bras lymphadénectomie) vs 12%, p=0.02





Radiothérapie - Quoi de neuf ? (2021)

Marnitz et al. Int J Gynecol Cancer -2020

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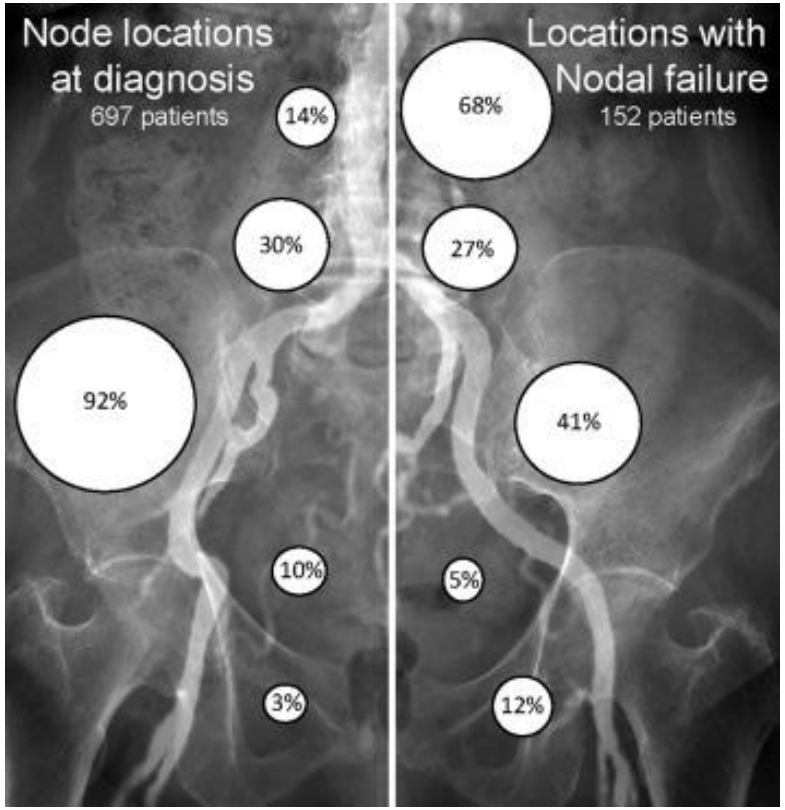
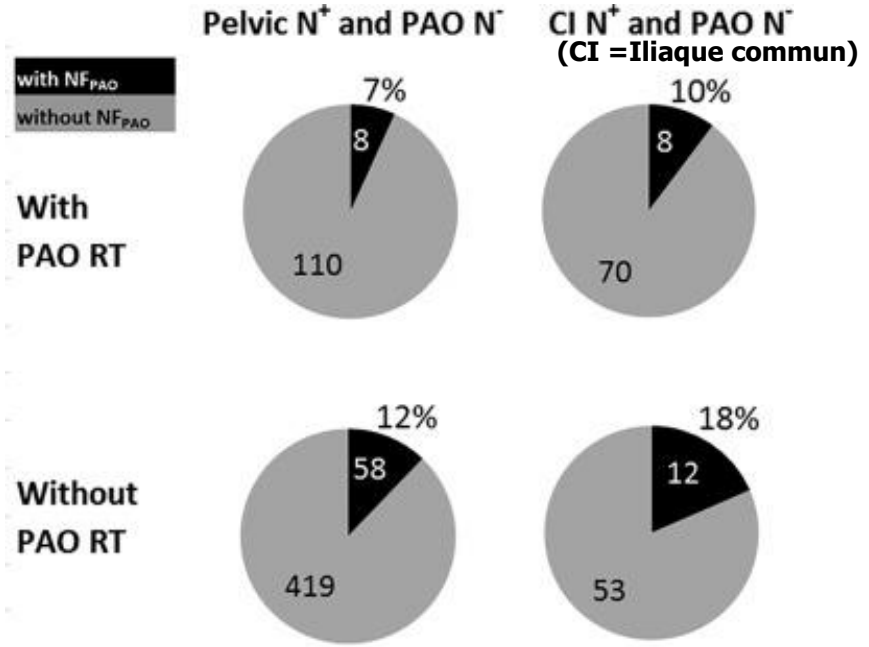
RECHUTE GANGLIONNAIRE

Taux de contrôle ganglionnaire à 3 ans et 5 ans: 87% et 86%
À 3 ans: 92% patientes N0- vs 82% patientes N+, p<0.001

24% des rechutes ganglionnaires sont associées à une rechute locale





Radiothérapie - Quoi de neuf ? (2021)

Nomden et al. Radiotherapy and Oncology 2019

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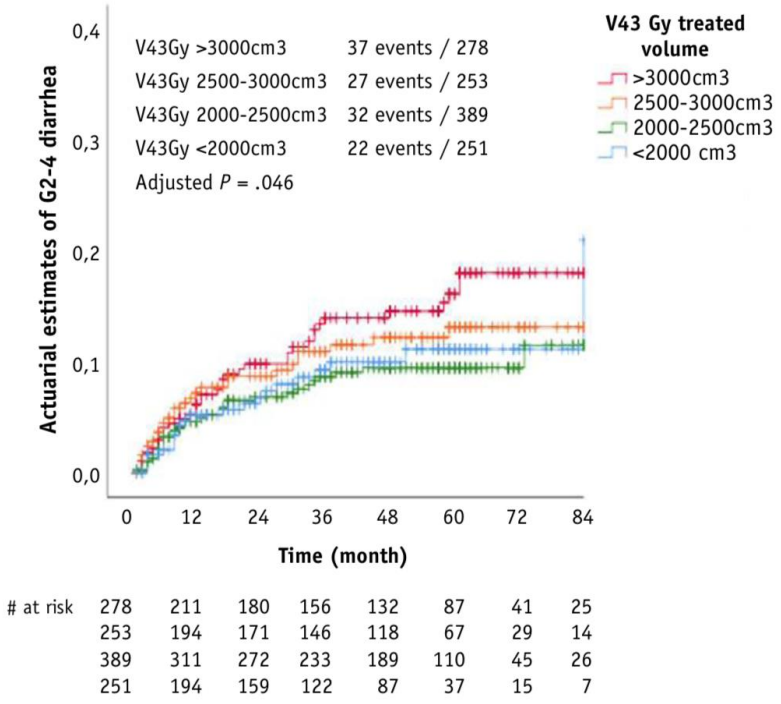
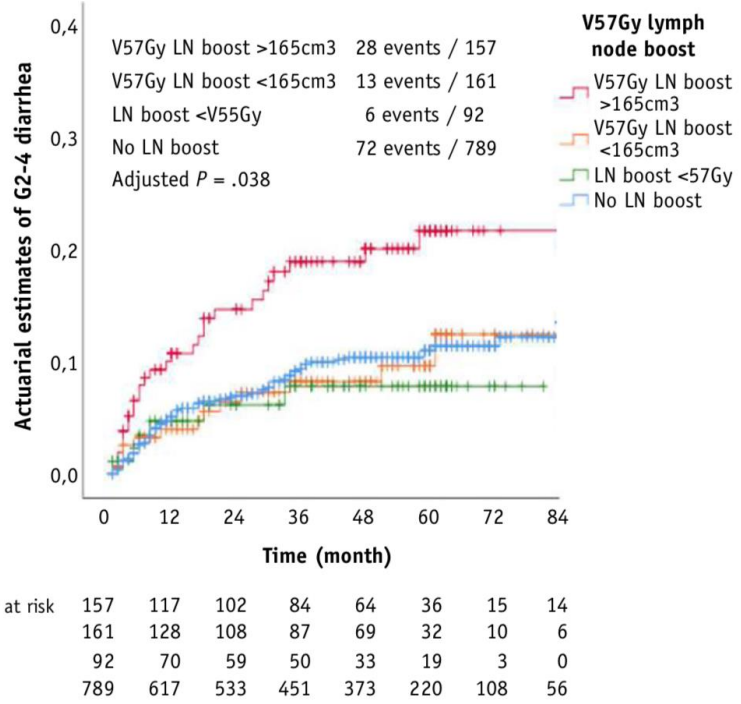
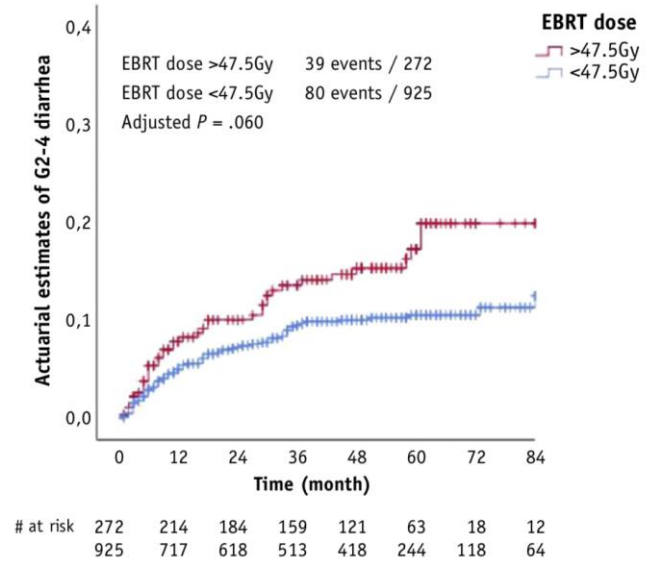
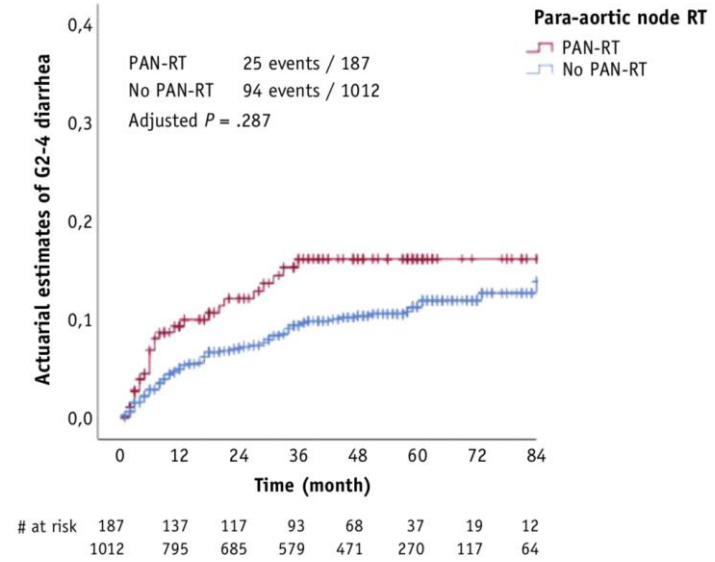
TOXICITÉ DIGESTIVE









Radiothérapie - Quoi de neuf ? (2021)

Jensen et al. Int J Radiation Oncol Biol Phys- 2021

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QUEL VOLUME/DOSES DE RADIOTHÉRAPIE EXTERNE ?

Irradiation lomboaortique prophylactique ?

- Indication ajustée au résultat du staging chirugical (notamment en cas d'atteinte des paramètres)
- Et/ou indication adaptée au risque ganglionnaire

Risque ganglionnaire	Stades	Volume ganglionnaire prophylactique
Bas risque	stades IA IB1,IIA1, taille < 4 cm, N0, pas d'extension utérine C. épidermoïdes	Petit pelvis = iliaques internes; externes, obturateurs, pré-sacrés
Risque intermédiaire		Pelvis large (= petits pelvis + iliaque primitif, incluant la bifurcation aortique)
Haut risque	≥ 3 ganglions ≥ 1 ganglion iliaque commun	Pelvis large + LAO jusqu'à la veine rénale G ou + 3cm au dessus de l'atteinte macroscopique ganglionnaire

Optimisation dosimétrique ?

- Marges de PTV du CTV-E réduites à 5 mm
- Dose de radiothérapie externe limitée à 45 Gy
- IGRT quotidienne voire radiothérapie adaptative
- Boost intégré ganglionnaire
- Optimiser le V57 Gy du boost : CovP (coverage probability dose planning)

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MERCI
www.onco-nouvelle-aquitaine.fr