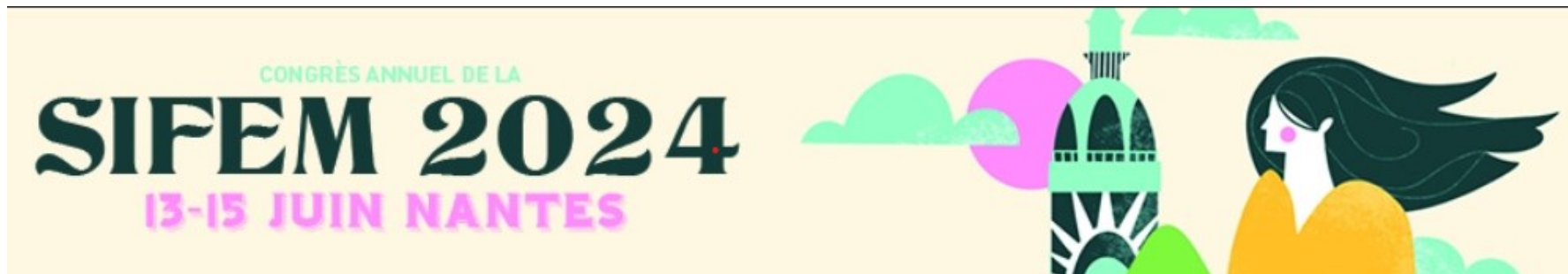


Nouvelles recommandations pour la prise en charge des cancers de l'endomètre

Intégration de la classification FIGO 2023

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Pas de conflit d'intérêt



Introduction



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JGO
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FIGO Staging Update



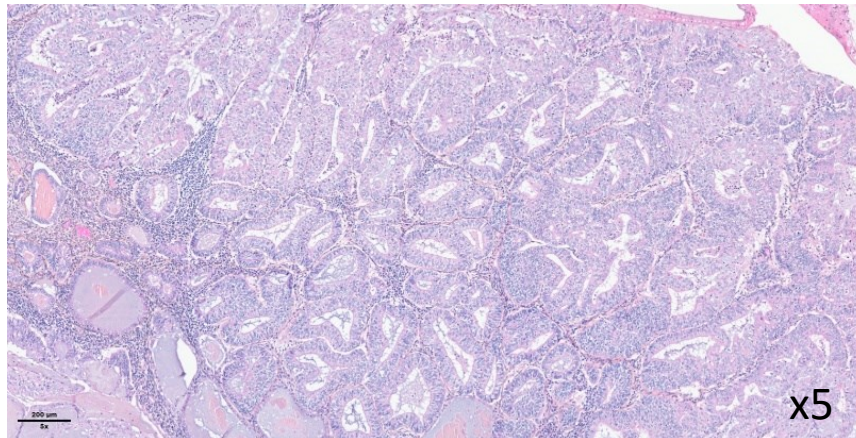
FIGO staging of endometrial cancer: 2023

Jonathan S. Berek ¹ Xavier Matias-Guiu ² Carien Creutzberg ³
 Christina Fotopoulou ⁴ David Gaffney ⁵ Sean Kehoe ⁶ Kristina Lindemann ⁷
 David Mutch ⁸ Nicole Concin ^{9,10} Endometrial Cancer Staging Subcommittee,
 FIGO Women's Cancer Committee

- Nouvelle classification FIGO parue en 2023 (version précédente : 2009 modifiée en 2018)
 - Reste basée sur l'analyse pathologique de la pièce opératoire
 - Découle largement des recommandations **ESGO/ESTRO/ESP 2021**
 - Intègre la classifications moléculaire du Cancer Genome Atlas (TCGA)
- Rôle toujours central de l'imagerie dans le bilan d'extension locorégional préopératoire, à réadapter à la lumière de cette classification

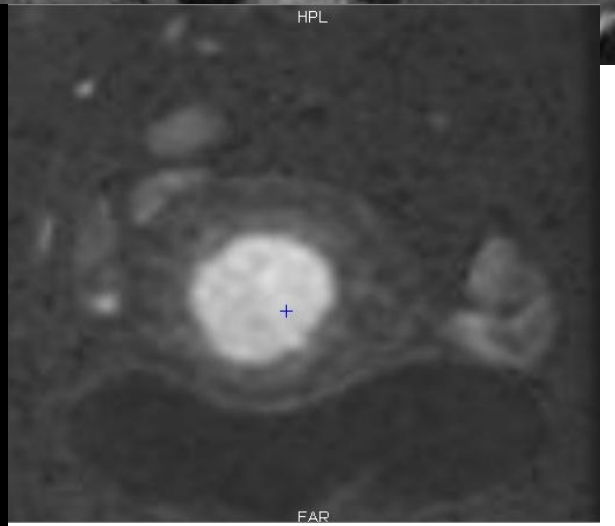
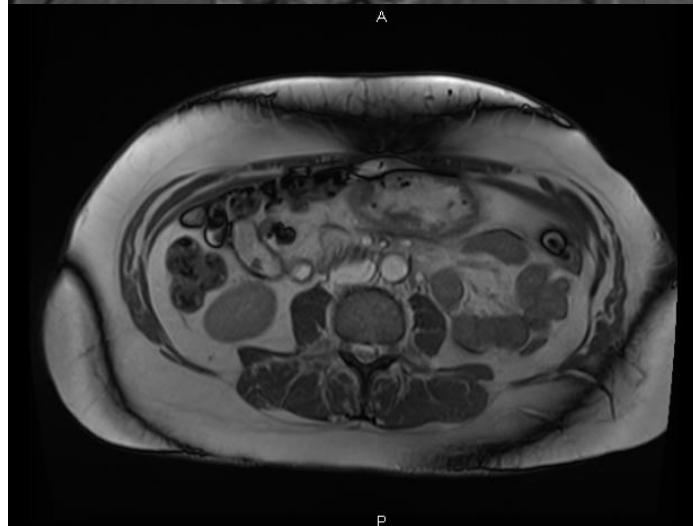
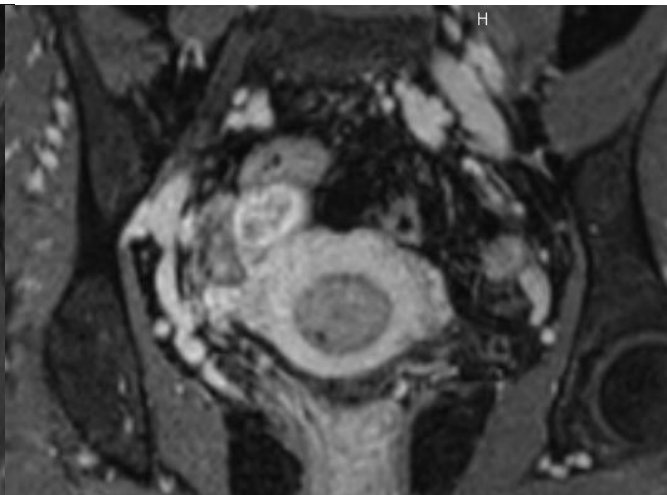
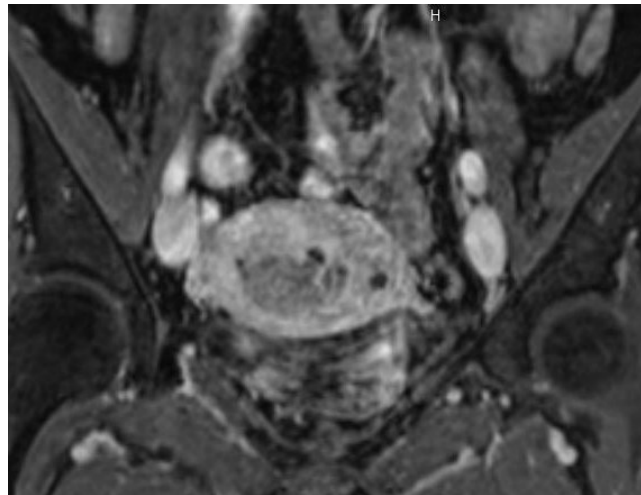
Cas clinique

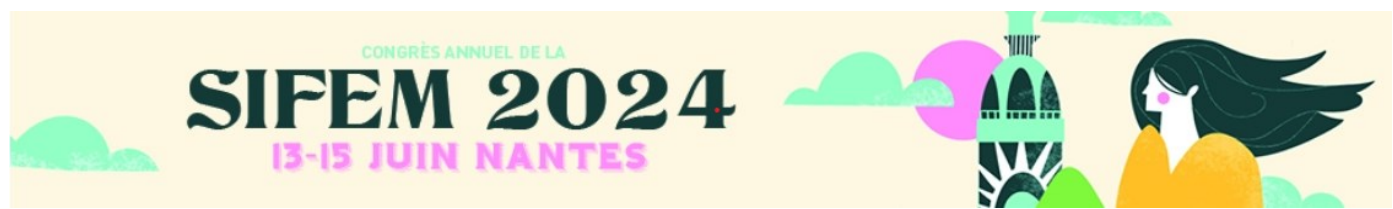
- Métrorragies post-ménopausique chez une patiente de 62 ans depuis quelques mois
- Biopsie de l'endomètre (pipelle de Cornier) : adénocarcinome endométrioïde de bas grade (grade 1), absence d'embolies vasculaires



*Image Dr C. Pasquesoone
Centre Oscar Lambret*

- IRM pelvienne et lombo-aortique pour bilan d'extension locorégional initial





- Quels éléments clés du bilan d'extension devez vous préciser ?
- Comment formuler la conclusion de votre compte rendu ?

- CAT thérapeutique proposée ?

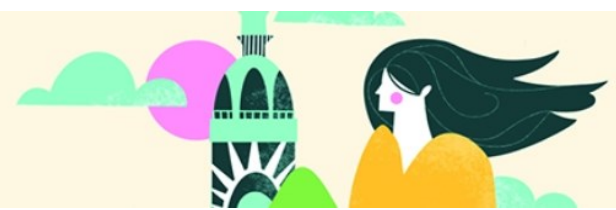


Table 2 Definition of prognostic risk groups

Risk group	Molecular classification unknown
Low	▶ Stage IA endometrioid + 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, 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
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
Advanced metastatic	▶ Stage III–IVA with residual disease ▶ Stage IVB

Hystérectomie totale avec annexectomie bilatérale

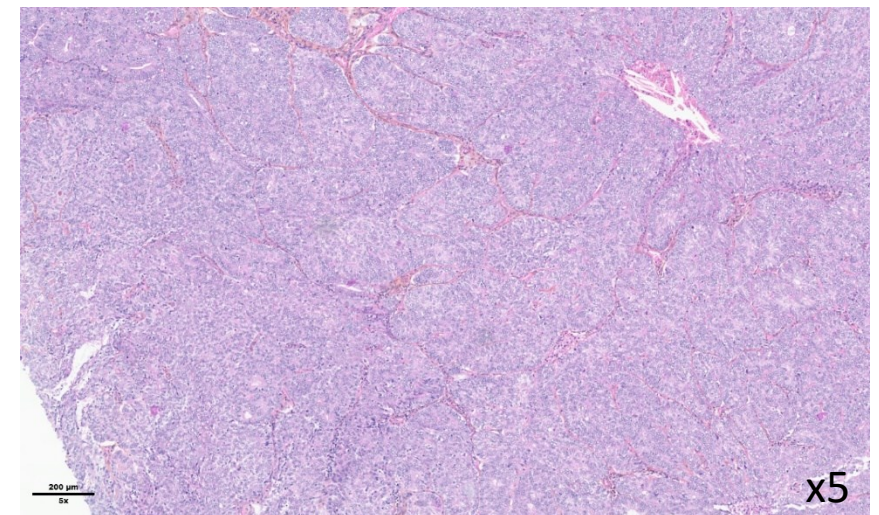
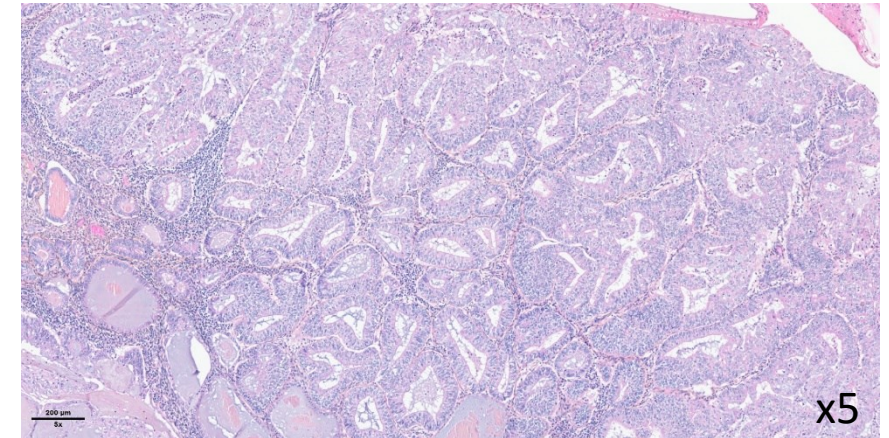
- Analyse du GS validée
- GS omis si forme intramuqueuse

- Analyse du GS possible, sinon curage pelvien et LA d'emblée

Analyse histologique de la pièce d'HTAB+ GS

- Adénocarcinome endométrioïde de haut grade (grade 3)
- Emboles vasculaires significatifs (> à 5)
- Infiltration du myomètre inférieure à 50 % de son épaisseur

**Re-stadification post opératoire
et implications thérapeutiques?**



SPECIAL ARTICLE

Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up[☆]

A. Oaknin¹, T. J. Bosse², C. L. Creutzberg³, G. Giordano⁴, P. Harter⁵, F. Joly^{6,7}, D. Lorusso^{8,9}, C. Marth¹⁰, V. Makker^{11,12}, M. R. Mirza¹³, J. A. Ledermann^{14,15} & N. Colombo^{16,17}, on behalf of the ESMO Guidelines Committee^{*}

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Advanced metastatic	▶ Stage III–IVA with residual disease ▶ Stage IVB

- Pas de traitement adjuvant

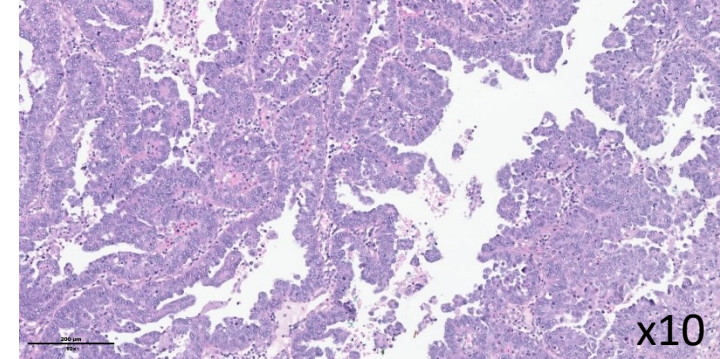
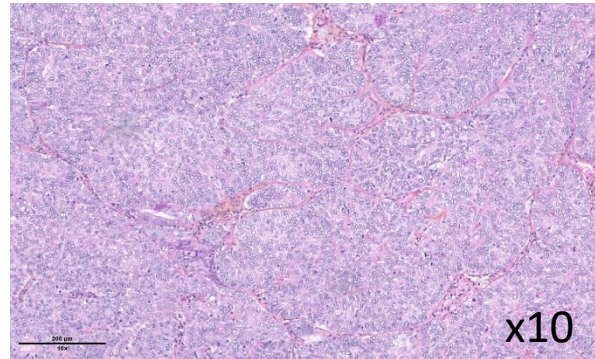
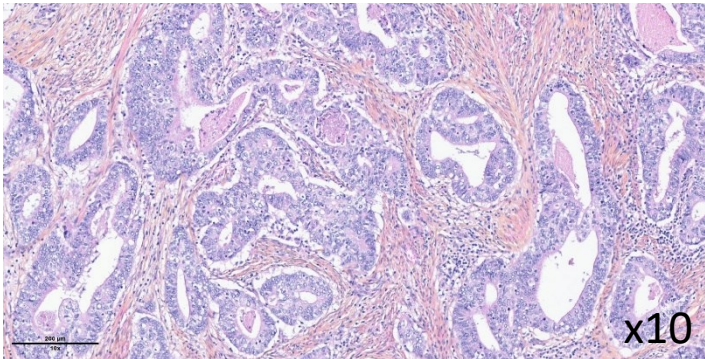
- Curiethérapie adjuvante recommandée
- Peut être omise si < 60 ans

- Curiethérapie adjuvante recommandée
- Radiothérapie externe
- Chimiothérapie adjuvante envisagée (grade 3 et LVSI significatives)

- Radio-chimiothérapie concomitante ou séquentielle
- Chimiothérapie exclusive

Problème: discordance entre groupes de risque pré /post-opératoires

- Discordance entre biopsie préopératoire / examen anatomopathologique définitif :
 - Différence de type histologique : 15%
 - Différence de grade tumoral dans le groupe des tumeurs endométrioïdes: 30 %



Images Dr C. Pasquesoone
Centre Oscar Lambret

Frumovitz M., Singh D.K., Meyer L., Smith D.H., Wertheim I., Resnik E., et al. Predictors of final histology in patients with endometrial cancer Gynecol Oncol 2004 ; 95 (3) : 463-468

Phelippeau J., Canlorbe G., Bendifallah S., Naoura I., Lefevre M., Ballester M., et al. Preoperative diagnosis of tumor grade and type in endometrial cancer by pipelle sampling and hysteroscopy: results of a French study Surg Oncol 2016 ; 25 (4) : 370-377



Et l'analyse moléculaire ..?

Réalisée sur pièce opératoire: **profil moléculaire p53 muté**

SUITE DU COMPTE RENDU N° 2403209

- Anticorps anti-P53 : marquage nucléaire intense des cellules tumorales en faveur d'un profil muté.
- Anticorps anti-Cytokératine AE1/AE3 : marquage cytoplasmique de 10% des cellules tumorales.
- Anticorps anti-EMA : marquage membranaire de 1% des cellules tumorales.
- Anticorps anti-MLH1, PMS2, MSH2 et MSH 6 : marquage nucléaire des cellules tumorales

Implications thérapeutiques?

SPECIAL ARTICLE

Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up[☆]

A. Oaknin¹, T. J. Bosse², C. L. Creutzberg³, G. Giordano⁴, P. Harter⁵, F. Joly^{6,7}, D. Lorusso^{8,9}, C. Marth¹⁰, V. Makker^{11,12}, M. R. Mirza¹³, J. A. Ledermann^{14,15} & N. Colombo^{16,17}, on behalf of the ESMO Guidelines Committee^{*}

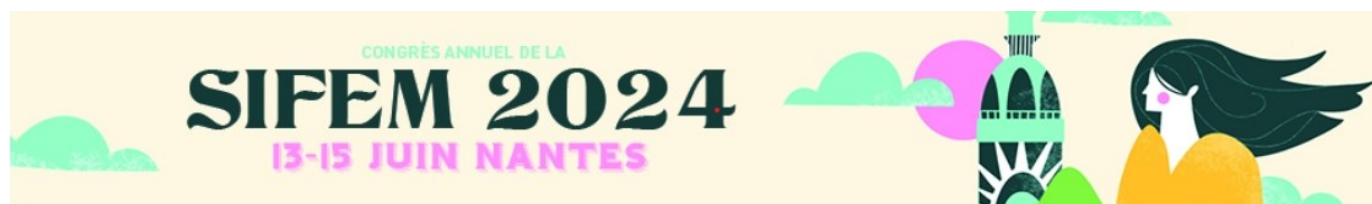
Table 2 Definition of prognostic risk groups

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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, undifferentiated 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

- Radio-chimiothérapie concomitante ou séquentielle
- Chimiothérapie exclusive

Concin N, Matias-Guiu X, Vergote I, et al

ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma International Journal of Gynecologic Cancer 2021;31:12-39.



FIGO staging of endometrial cancer: 2023

Table 1. 2023 FIGO staging of cancer of the endometrium*†

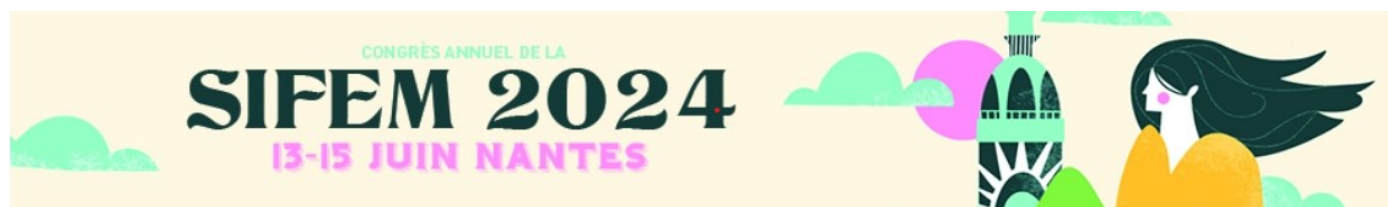
Stage	Description
Stage I	Confined to the uterine corpus and ovary [‡]
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e., low-grade endometrioid, with invasion of less than half of myometrium with no or focal LVSI OR good prognosis disease
IA1	Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
IA2	Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI
IA3	Low-grade endometrioid carcinomas limited to the uterus and ovary [‡]
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI [§]
IC	Aggressive histological types [¶] limited to a polyp or confined to the endometrium
Stage II	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI [§] of non-aggressive histological types
IIC	Aggressive histological types [¶] with any myometrial involvement

Pas de traitement adjuvant/ surveillance

« Stade I A »

Radiothérapie adjuvante+ chimiothérapie

« Stade IIC p53 abn »



Nouvelle classification FIGO 2023

- Illustre de la stratification en groupe de risques *des ESGO/ESTRO/ESP guidelines*
- **Facteurs pronostics histomoléculaires directement intégrés +++**
- CAT adjuvante plus « directe »

Principales nouveautés: intégration des LVSI

Table 1. 2023 FIGO staging of cancer of the endometrium*†

Stage	Description
Stage I	Confined to the uterine corpus and ovary [‡]
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e., low-grade endometrioid, with invasion of less than half of myometrium with no or focal LVSI OR good prognosis disease
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Stage II	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI [§] of non-aggressive histological types
IIC	Aggressive histological types [¶] with any myometrial involvement

LVSI as defined in WHO 2021: extensive/substantial, ≥5 vessels involved

Berek JS et al . FIGO staging of endometrial cancer: 2023. *J Gynecol Oncol.* 2023 Sep;34(5):e85.

WHO Classification of Tumours Editorial Board. *Female genital tumours, WHO classification of tumours. Vol. 4. 5th ed. Lyon: IARC Press; 2020.*

Principales nouveautés: intégration du sous-type histologique et du grading

Table 1. 2023 FIGO staging of cancer of the endometrium*†

Stage	Description
Stage I	Confined to the uterine corpus and ovary‡
IA	Disease limited to the endometrium OR <u>non-aggressive histological type</u> , i.e., low-grade endometrioid, with invasion of less than half of myometrium with no or focal LVSI OR good prognosis disease
IA1	Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
IA2	Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI
IA3	Low-grade endometrioid carcinomas limited to the uterus and ovary‡
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI§
IC	Aggressive histological types [¶] limited to a polyp or confined to the endometrium
Stage II	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR <u>aggressive histological types with myometrial invasion</u>
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI§ of non-aggressive histological types
IIC	Aggressive histological types [¶] with any myometrial involvement

- **Types histologiques agressifs** : adénocarcinomes endométrioides de haut grade (G3), carcinomes de type séreux, à cellules claires, carcinosarcomes, indifférenciés, mixtes et types inhabituels (mesonephric-like; and gastrointestinal mucinous type carcinomas)
- **Types histologiques non agressifs** : adénocarcinomes endométrioides de bas grade (G1 et G2)

Principales nouveautés: intégration de la classification moléculaire

4 sous groupes moléculaires du Cancer Genome Atlas (TCGA):

Tableau 1 Description des différents sous-types de cancer de l'endomètre.

	ADN polymérase epsilon (POLE) ultramutée	Défaut du système MMR	P53 muté	Profil moléculaire non spécifique (NSMP)
Prévalence	5–15 %	25–30 %	5–15 %	30–40 %
Profil clinique	Âge plus jeune	Syndrome de Lynch	Stades évolués au moment du diagnostic	Indices de masse corporelle plus élevés
Profil histologique	Souvent haut grade Infiltrat lymphocytaire important	Souvent haut grade Infiltrat lymphocytaire important Emboles vasculaires Mucineux	Haut grade Atypies prononcées Pas seulement les séreux	Bas grade
Pronostic	Excellent, indépendamment du stade	Intermédiaire (dépend du stade)	Mauvais (indépendamment du stade)	Intermédiaire (dépend du stade)
Perspectives de traitements	Désescalade	Immunothérapie	Inhibiteurs de la poly(ADP-ribose) polymérase	Piste antihormonale

MMR : mismatch repair.

Principales nouveautés: intégration de la classification moléculaire

Table 2. FIGO endometrial cancer stage with molecular classification*

Stage designation	Molecular findings in patients with early endometrial cancer (Stages I and II after surgical staging)
Stage IA _{m^{pOLEmut}}	POLEmut endometrial carcinoma, confined to the uterine corpus or with cervical extension, regardless of the degree of LVSI or histological type
Stage IIC _{m^{p53abn}}	p53abn endometrial carcinoma confined to the uterine corpus with any myometrial invasion, with or without cervical invasion, and regardless of the degree of LVSI or histological type

Berek JS et al . FIGO staging of endometrial cancer: 2023. J Gynecol Oncol. 2023 Sep;34(5):e85.

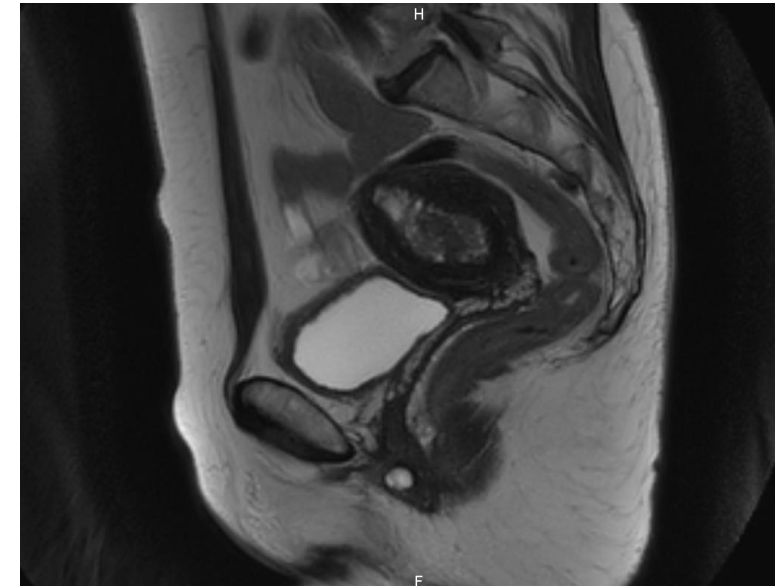
- Adjonction **recommandée** de la classification moléculaire
- **Modification du stade FIGO uniquement si stade I ou II (sur pièce op) avec mutation p53 ou POLE mut**
 - A consigner dans tous les autres cas à visée de collecte de données, mais ne change pas la classification
 - Si biologie moléculaire réalisée sur biopsie: inutile de la répéter

Principales nouveautés «radiologiques»

- Individualisation d'une forme polypoïde / confinée à l'endomètre : **stade IA1**

Table 1. 2023 FIGO staging of cancer of the endometrium*†

Stage	Description
Stage I	Confined to the uterine corpus and ovary‡
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e., low-grade endometrioid, with invasion of less than half of myometrium with no or focal LVSI OR good prognosis disease
	<u>IA1 Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium</u>
	IA2 Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI
	IA3 Low-grade endometrioid carcinomas limited to the uterus and ovary‡
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI§
IC	Aggressive histological types¶ limited to a polyp or confined to the endometrium



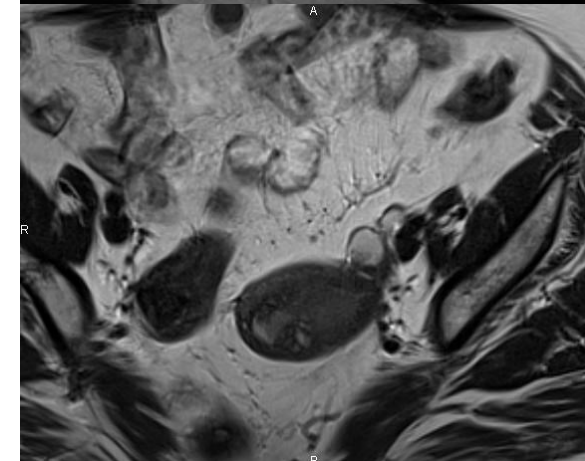
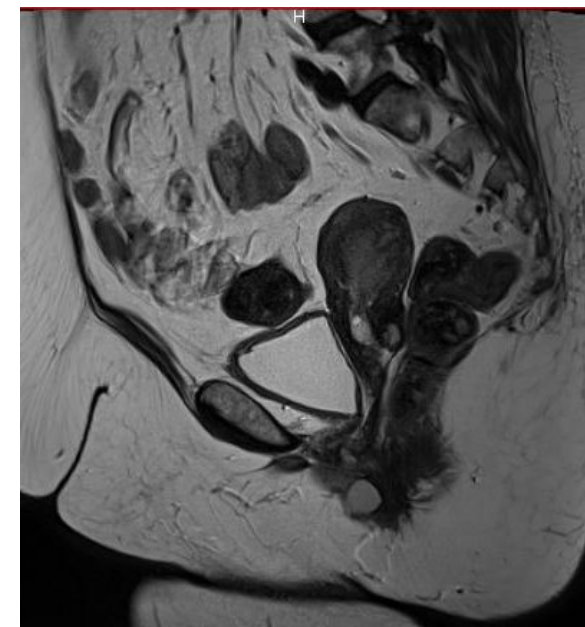


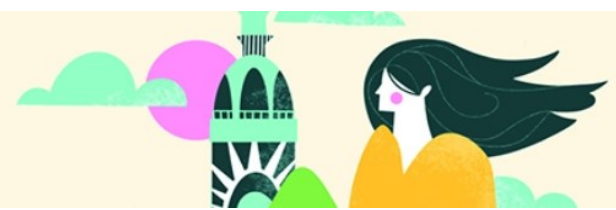
Principales nouveautés «radiologiques»

- Détermination de tumeurs endométriales et annexielles synchrones: **stade IA3 en cas de bas grade**

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Stage	Description
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IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI§
IC	Aggressive histological types¶ limited to a polyp or confined to the endometrium





Principales nouveautés «radiologiques»

- **Stades avancés : III et IV**

Stage III Local and/or regional spread of the tumor of any histological subtype

IIIA Invasion of uterine serosa, adnexa, or both by direct extension or metastasis

IIIA1 Spread to ovary or fallopian tube (except when meeting stage IA3 criteria)[‡]

IIIA2 Involvement of uterine subserosa or spread through the uterine serosa

IIIB Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum

IIIB1 Metastasis or direct spread to the vagina and/or the parametria

IIIB2 Metastasis to the pelvic peritoneum

IIIC Metastasis to the pelvic or para-aortic lymph nodes or both[¶]

IIIC1 Metastasis to the pelvic lymph nodes

IIIC1i Micrometastasis

IIIC1ii Macrometastasis

IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes

IIIC2i Micrometastasis

IIIC2ii Macrometastasis

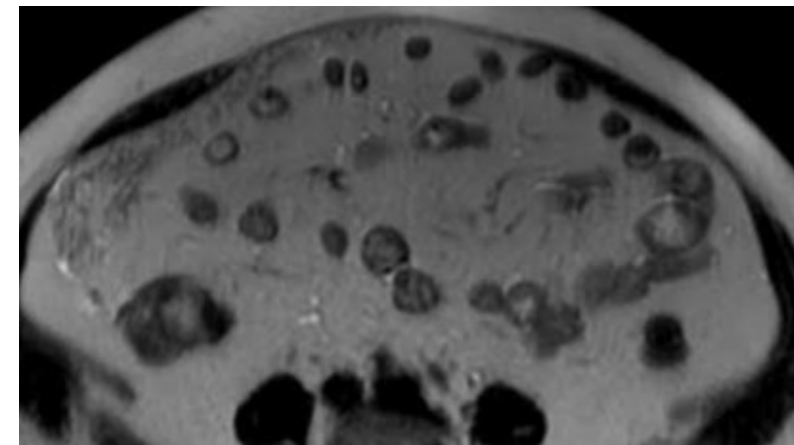
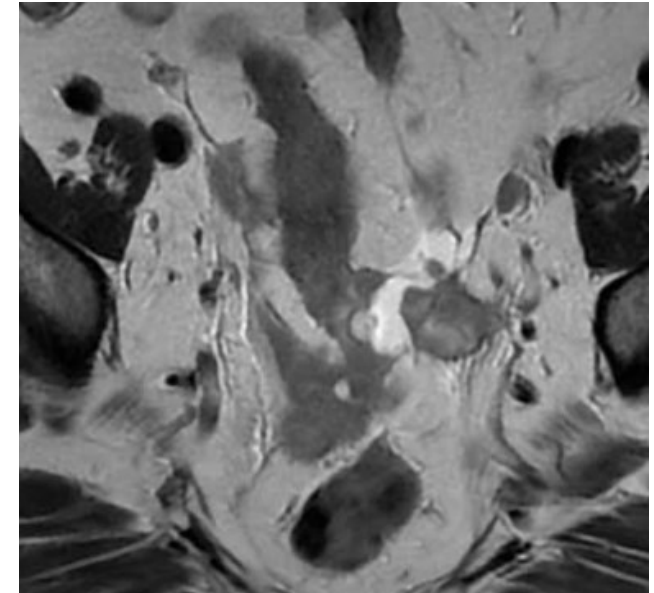
Stage IV Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis

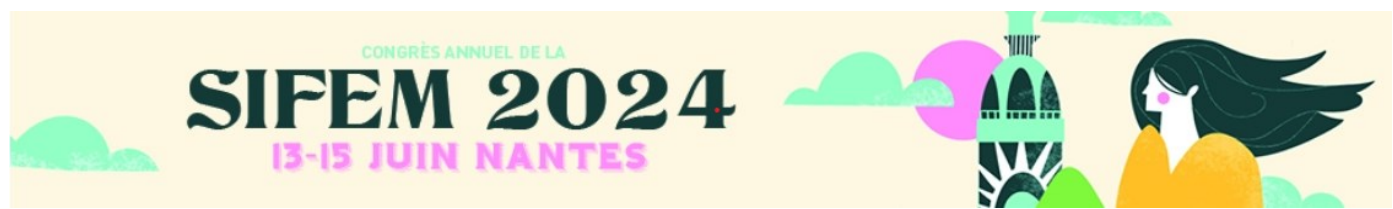
IVA Invasion of the bladder mucosa and/or the intestinal/bowel mucosa

IVB Abdominal peritoneal metastasis beyond the pelvis

IVC Distant metastasis, including metastasis to any extra-or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

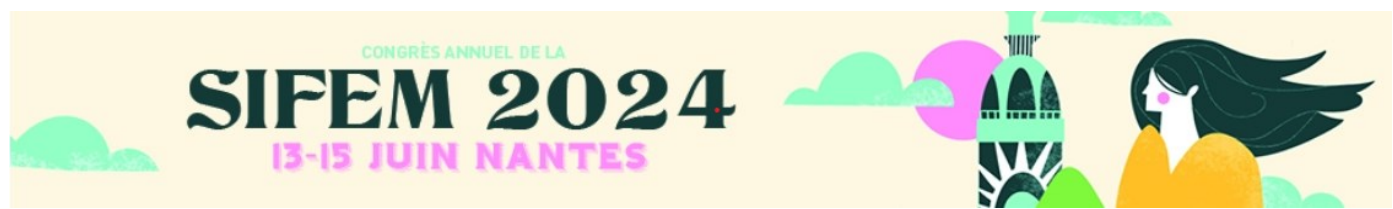
- **stade IIIA1 ≠ IIIA2**
- Dissemination péritonéale: **stade IIIB2**
- **IIIC**: différenciation micro/ macrométastases
- Adjonction **stade IV B**





Conclusions

- « Intégration » directe dans la classification des modifications récentes déjà prises en compte ces dernières années pour les indications de traitements adjuvants
- Rôle majoré de nos collègues anatomopathologistes : type histologique, grade, LVSI, biologie moléculaire directement intégrés ...



Conclusions

- Pas au détriment d'une réduction de notre rôle dans le bilan !
 - Éléments sémiologiques de l'ancienne classification à conserver mais **plus de sens à l'élaboration d'une classification « FIGO-IRM »**
 - Principales nouveautés radiologiques ... à intégrer dans le CR-type: formes polypoïdes, tumeurs synchrones annexe/ endomètre , péritoine pelvien

CONGRÈS ANNUEL DE LA

SIFEM 2024

LA CITE DES CONGRES
DE NANTES

IMAGERIE DE LA FEMME VOIR PLUS LOIN

ISABELLE DOUTRIAUX-DUMOULIN
LAURENCE VILCOT
DELPHINE GEFFROY

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