# Small cell carcinomas of the genital tract: ovary vs cervix

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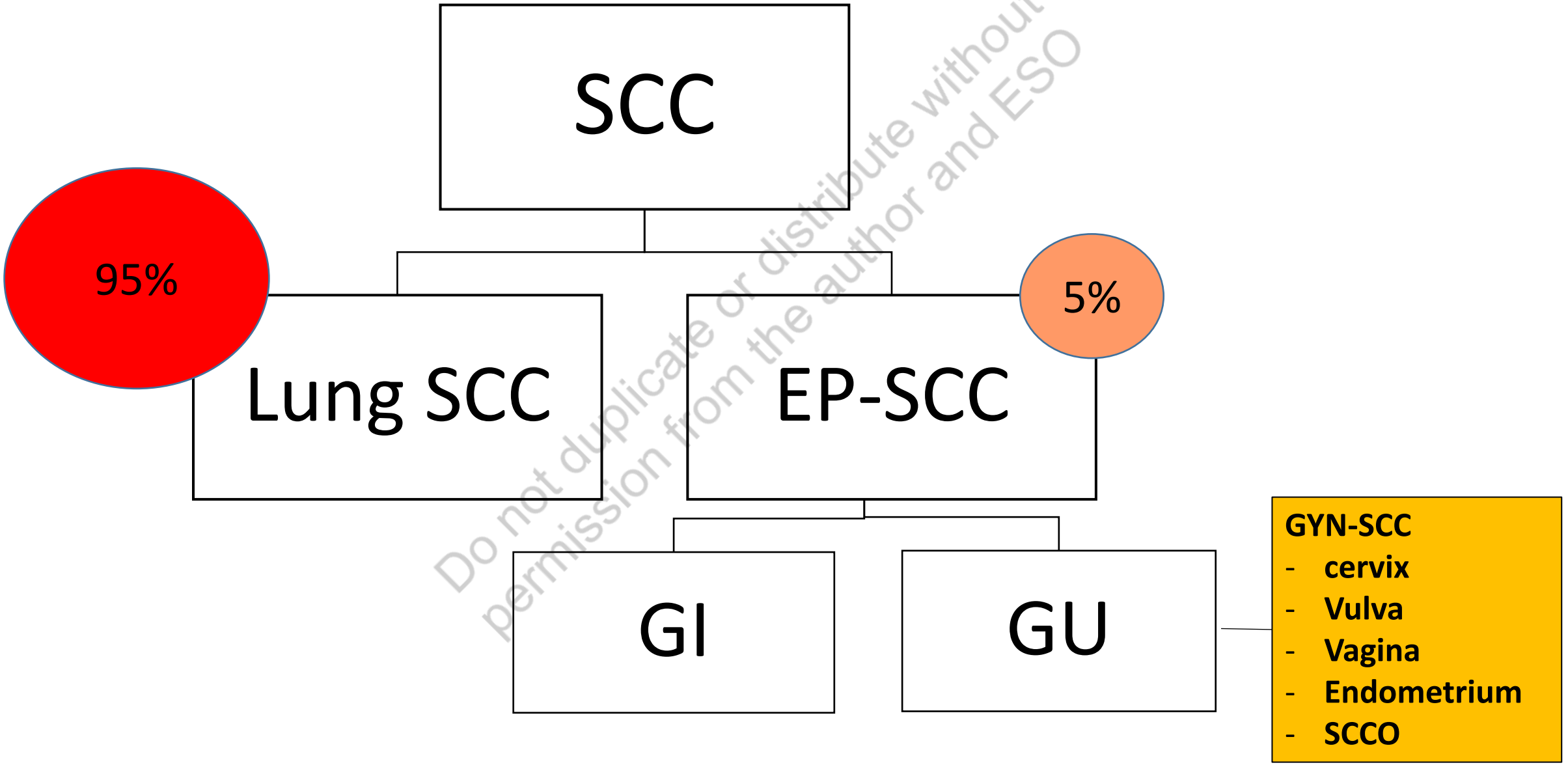
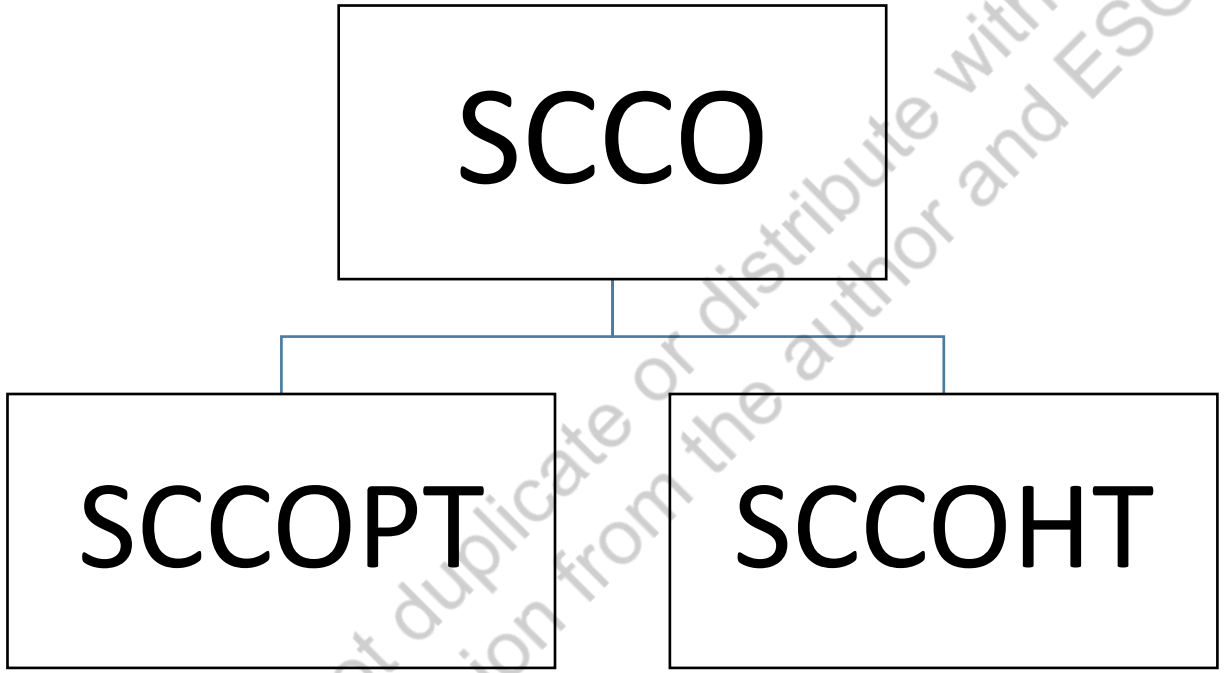
# Extrapulmonary small cell carcinomas



# SCCO classification




SCCO pulmonary type

SCCO hypercalcemic type

The only gyn SCC not belonging to NECs

# SCCOPT

**Extremely rare – few cases reported in literature**
**not possible to make recommendations!**

- Present in women with a mean age of 51 (22-81 years)
- 50% bilateral disease

- PATHOLOGY: difficult to distinguish SCCOPT form SCC of the lung (metastatic vs primary?)
  - Neuroendocrine markers: Chr A, NSE, CD56, synaptophysin
- MOLECULAR FEATURES: BRCA2 (not pathogenic), TP53

- TREATMENT: surgery + chemotherapy (regimens derived from lung SCC)

| |
|---|
| Cisplatin/carboplatin + etoposide |
| Alkylating agents |
| Paclitaxel |
| Irinotecan |

*Patibandla JR et al. Gynecol Oncol 2018*

# SCCOHT - Epidemiology

- The only subtype of gyn SCC not belonging to NECs.

- First described in 1979 by Scully – fewer than 500 cases reported in literature
  - PATHOLOGY: Typical morphologic appearance of small hypercromatic cells with scant cytoplasm and brisk mitotic activity

  - Hypercalcemia present in 2/3 of the patients – expression of Parathyroid hormone-related protein

- It mainly affects adolescents and young women (mean age 24 years)



*Young et al., Am J Surg Pathol 1994*

# Clinical presentation

Presenting symptoms/signs:

- Abdominal pain
- Detection of abdominal mass
- Enlarged waist
- Nausea- Vomiting
- Weight loss



- Stage distribution

| | |
|---|---|
| I | 39% |
| II | 10% |
| III | 45% |
| IV | 6% |

*Witkoswki L et al., Gynecol Oncol 2016*

# Staging

| | | |
|---|---|---|
| I | Tumor confined to ovaries or fallopian tube(s) | T1 |
| IA | Tumor limited to one ovary (capsule intact) or fallopian tube, No tumor on ovarian or fallopian tube surface No malignant cells in the ascites or peritoneal washings | T1a |
| IB | Tumor limited to both ovaries (capsules intact) or fallopian tubes<br>No tumor on ovarian or fallopian tube surface<br>No malignant cells in the ascites or peritoneal washings | T1b |
| IC | Tumor limited to one or both ovaries or fallopian tubes, with any of the following:<br>IC1 Surgical spill intraoperatively<br>IC2 Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface<br>IC3 Malignant cells present in the ascites or peritoneal washings | T1c |
| II | Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer (Tp) | T2 |
| IIA | Extension and/or implants on the uterus and/or fallopian tubes/and/or ovaries | T2a |
| IIB | Extension to other pelvic intraperitoneal tissues | T2b |
| III | Tumor involves one or both ovaries, or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes | T3 |
| IIIA | Metastasis to the retroperitoneal lymph nodes with or without microscopic peritoneal involvement beyond the pelvis | T1,T2,T3aN1 |
| IIIA1 | Positive retroperitoneal lymph nodes only (cytologically or histologically proven) | |
| IIIA1(i) | Metastasis ≤ 10 mm in greatest dimension (note this is tumor dimension and not lymph node dimension) | T3a/T3aN1 |
| IIIA1(ii) | Metastasis > 10 mm in greatest dimension | |
| IIIA 2 | Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes | T3a/T3aN1 |
| IIIB | Macroscopic peritoneal metastases beyond the pelvic brim ≤ 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes | T3b/T3bN1 |
| III C | Macroscopic peritoneal metastases beyond the pelvic brim > 2 cm in greatest dimension, with or without metastases to the retroperitoneal nodes (Note 1) | T3c/T3cN1 |
| IV | Distant metastasis excluding peritoneal metastases<br>Stage IV A: Pleural effusion with positive cytology<br>Stage IV B: Metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of abdominal cavity) (Note 2)<br>(Note 1: includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)<br>(Note 2: Parenchymal metastases are Stage IV B) | Any T, Any N, M1<br>T3c/T3cN1) |

Notes:

1. Includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ.
2. Parenchymal metastases are Stage IV B.

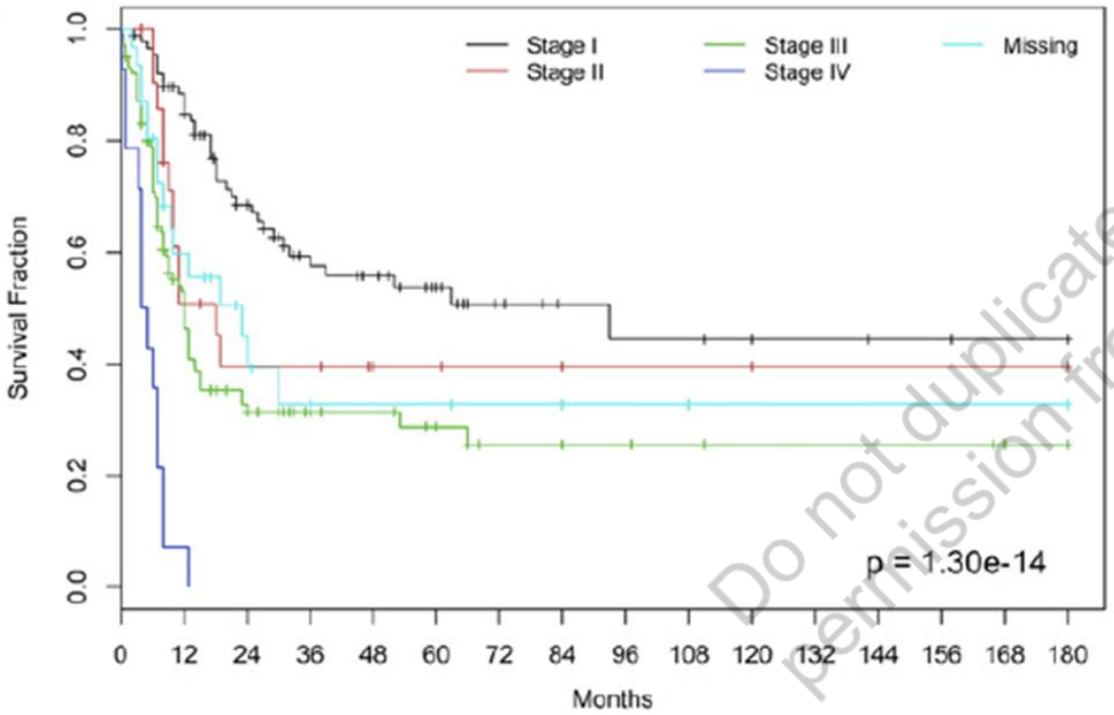


*Mutch D et al, Gynecologic Oncology, 2014*

# Prognosis

- Poor , 30-40% long term survivors with standard treatment

Even if initial responses to chemotherapy are frequent, chemoresistant relapses are common.





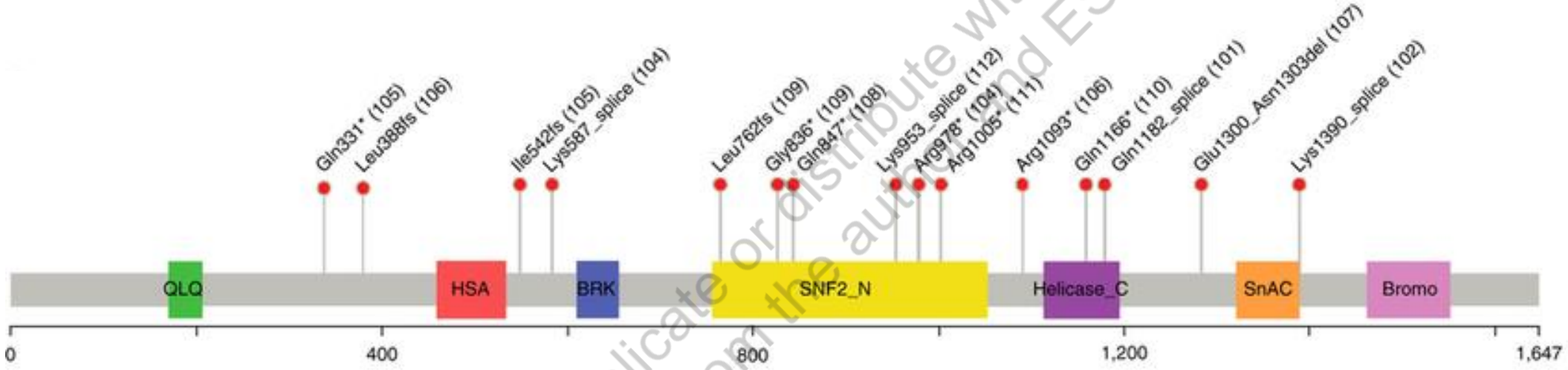

## PROGNOSTIC FACTORS

- STAGE (IA vs others)
- AGE (>30)
- Preoperative calcium levels (lower vs higher)
- Tumor size (<10 cm)
- Absence of large cells
- Optimal cytoreduction (vs TR>0)

*Reed NS et al, Int J Gynecol Cancer 2014*
*Bristow RE et al, J Clin Oncol 2002*
*Witkoswki L et al., Gynecol Oncol 2016*

# SCCOHT - Pathogenesis

SMARCA4 germline/somatic inactivating mutation → loss of function of SMARCA4/BRG1 protein
Present in 95% of SCCOHT






SMARCA4/BRG1 is part of the chromatin remodeling complex SWI/SNF that makes DNA accessible to transcriptional regulators/repressors

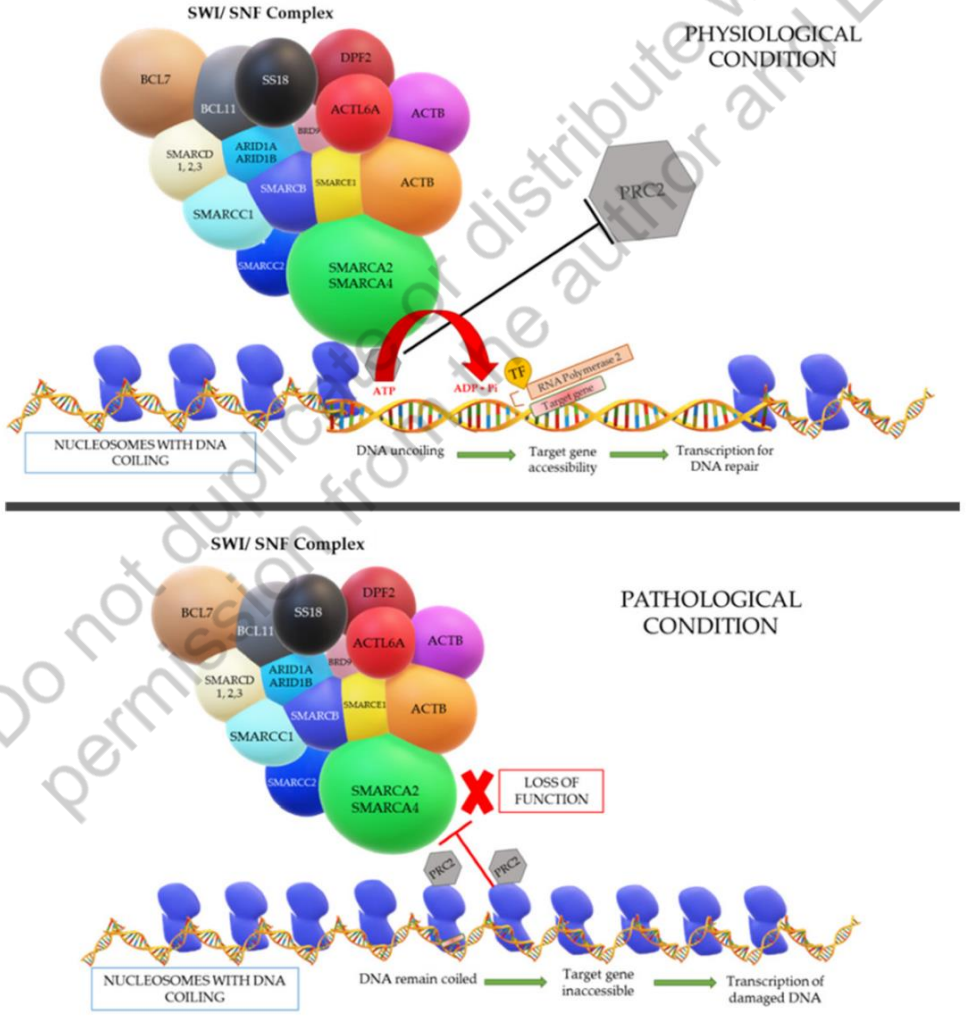
- DNA transcriptional regulation
- DNA damage repair
- Cell Differentiation
- Mitosis

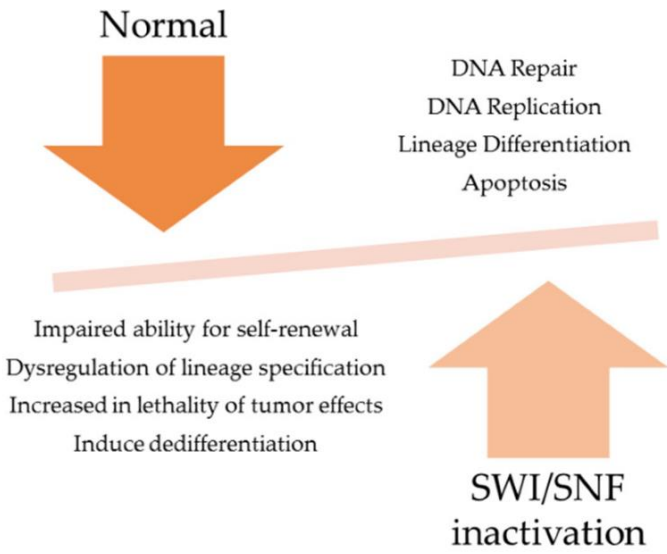
# SCCOHT - Pathogenesis

SMARCA4 and SMARCA2 are mutually exclusive tumor suppressors

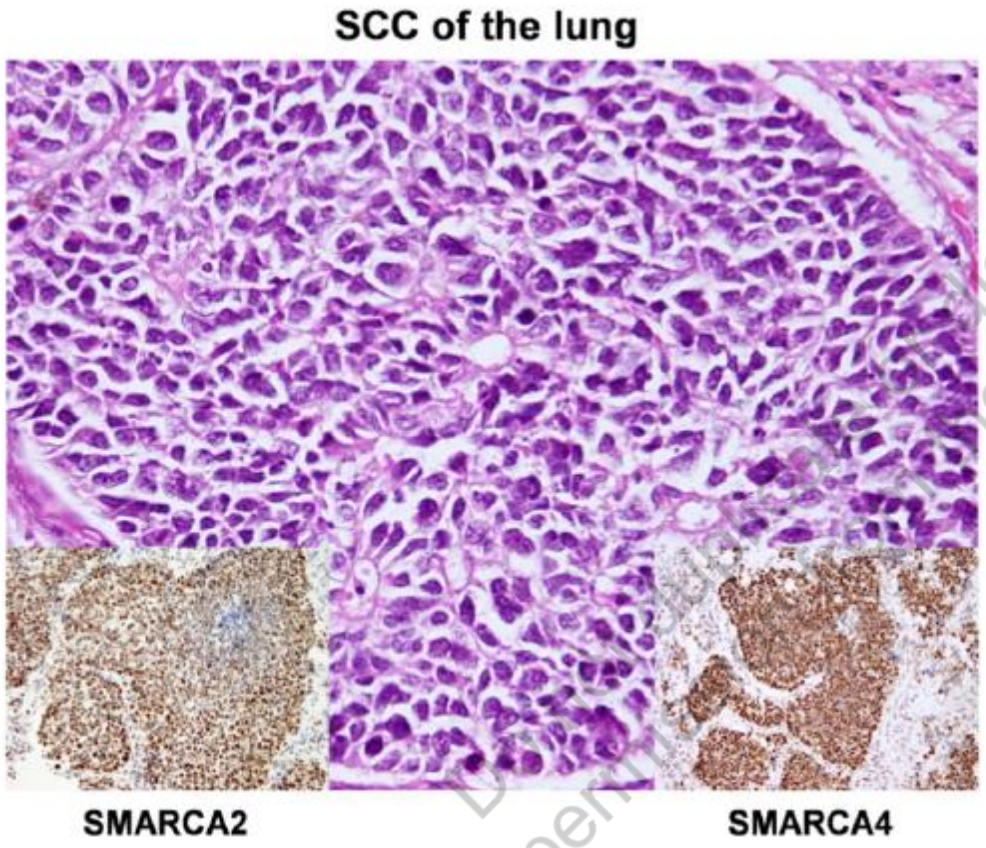
Occasionaly tumors exhibit loss of SMARCA2 and retention of SMARCA
4.

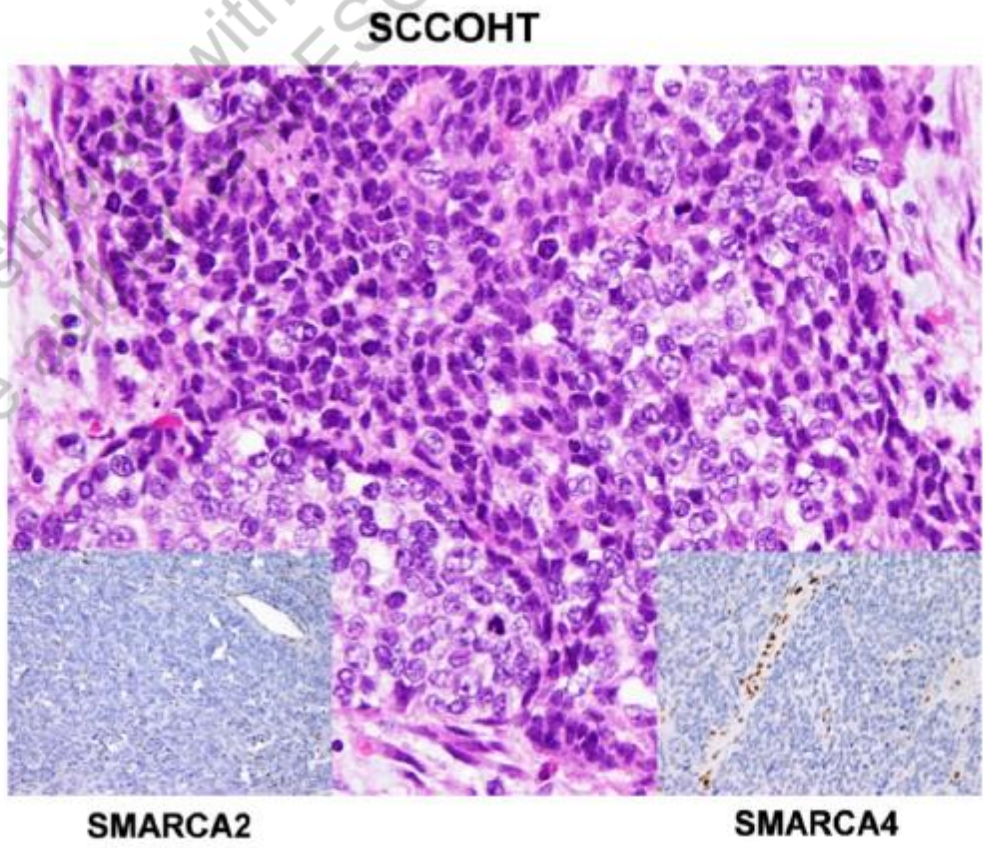
The concomitant loss of SMARCA4 and SMARCA2 (via epigenetic silencing) is **pathognomonic** of SCCOHT



# Pathology






*Patibandla et al., Gynecologic Oncology, 2018*

# Differential diagnoses

Ovarian Granulosa cell tumors

MOGCT

ESS

Neuroblastoma

**SMARCA4 IHC**
**Expert gyn pathologist**

Intraabdominal desmoplastic small round cell tumor

Lymphoma

Ovarian metastases melanoma/SCLC

# ISC recommendations on Genetic counselling

International SCCOHT Consortium

Molecular feature of SCCOHT is SMARCA4 germline/somatic inactivating mutation

Germline mutation(up to 40%): younger onset, family history generally silent

Risk of other tumors: uncertain

**Genetic Counseling**

- Refer all SCCOHT patients to a clinical genetics service and offer testing for germline *SMARCA4* PVs.
- Discuss risk-reducing contralateral oophorectomy in SCCOHT patients with a germline *SMARCA4* PV, due to increased risk of second primary malignancy.
- Tumor sequencing can confirm diagnosis and serve as a reference for germline sequencing. If no *SMARCA4* mutation is detected, SCCOHT diagnosis should be reconsidered.
- Germline sequencing without prior somatic sequencing can be performed where there is a confirmed diagnosis of SCCOHT through loss of SMARCA4 on IHC coupled with appropriate histologic findings.
- Offer genetic counseling and predictive testing to all at-risk relatives of SCCOHT patients with germline *SMARCA4* PVs.

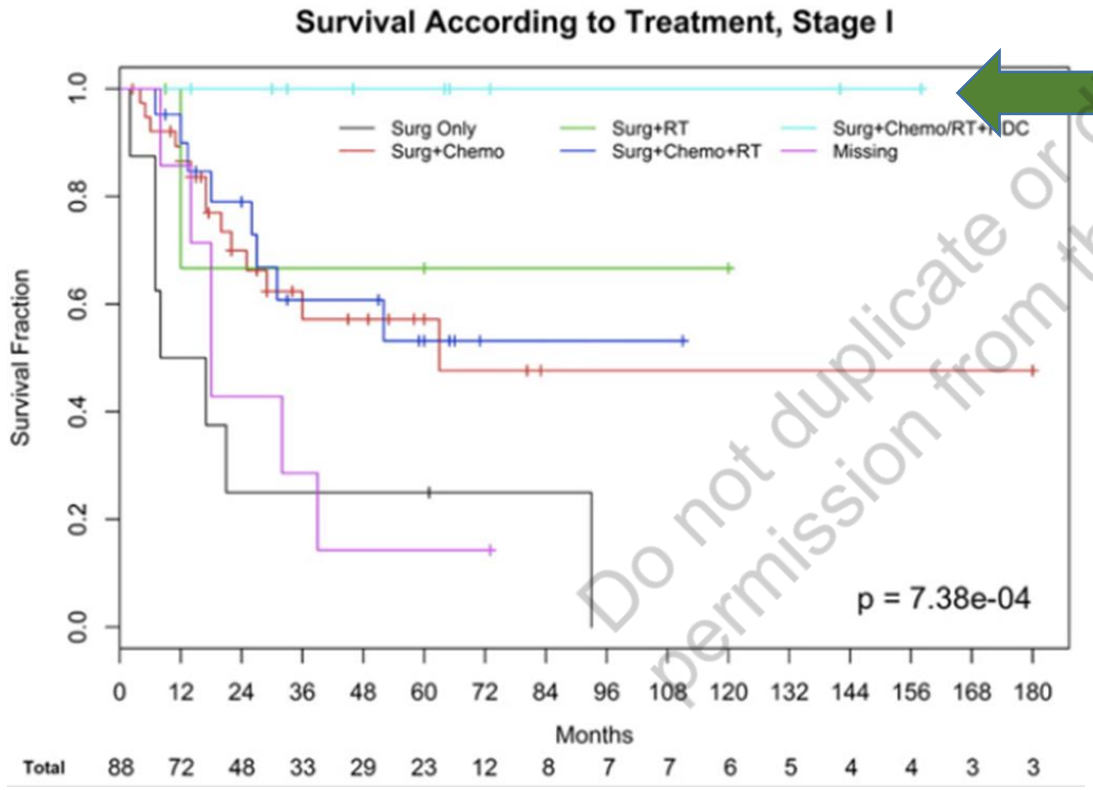


*Tischkowitz M et al. Clin Can Res 2020*

# Treatment

Lack of prospective studies – treatment based on retrospective case series with heterogeneous management

MULTIMODAL APPROACH RECOMMENDED






*Witkowski L et al., Gynecol Oncol 2016*
*Ray Coquard I et al., ESMO Guidelines, Ann Oncol 2018*
*Tischkowitz M et al. Clin Cancer Res 2020*

# Surgical treatment- stage I

| Author, year | Number cases total | Recurrences in USO | Recurrences in BSO |
|---|---|---|---|
| Young, 1994 | 150 | 16/21 | 6/14 |
| Callegaro Filho, 2015 | 47 | 6/8 | 4/8 |
| Total | 197 | 22/29 (75.8%) | 10/22 (45.4%) |

No pregnancies reported

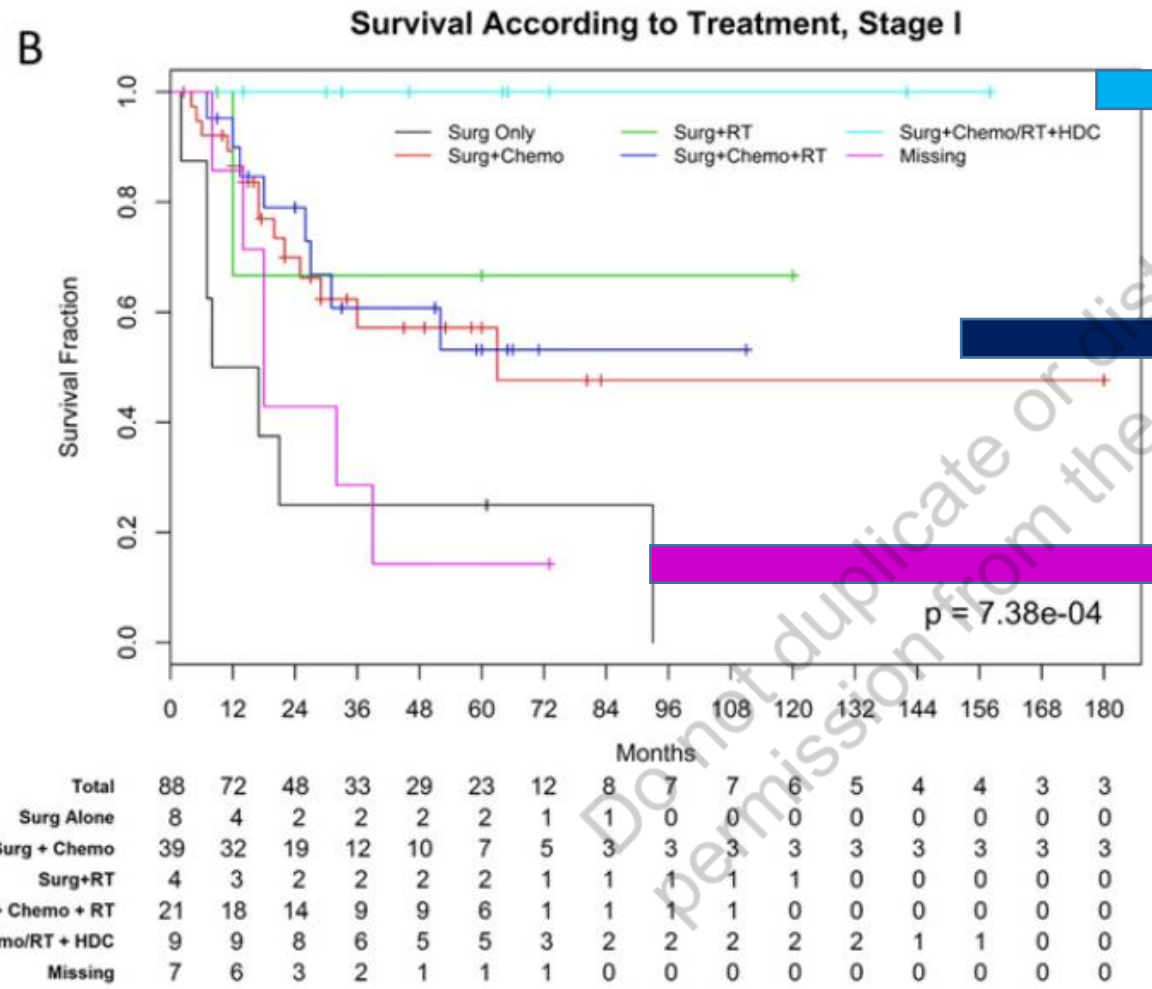
Gonadotoxic effect of chemotherapy



*Young et al., Am J Surgical Pathol 1994*

*Callegaro-Filho et al. Gynecol Oncol 2015*

# Treatment - stage I




Best outcome obtained with surgery+chemo/RT+ HDCT (100% OS on 9 patients)C

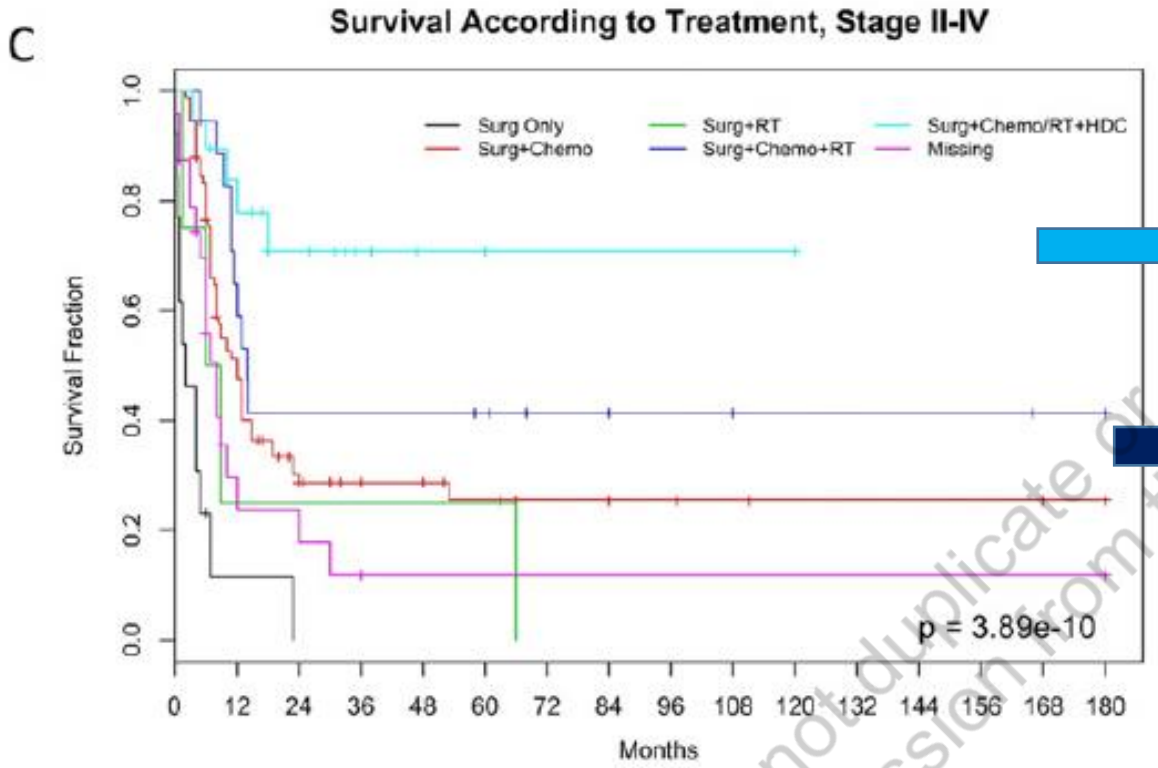
No advantage of adding RT to surgery+chemo

Surgery alone: worse prognosis



*Witkowski L et al., Gynecol Oncol 2016*
*Ray Coquard I et al., ESMO Guidelines, Ann Oncol 2018*
*Tischkowitz M et al. Clin Cancer Res 2020*

# Treatment - stage II-IV




| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total | 169 | 73 | 40 | 27 | 22 | 18 | 12 | 12 | 9 | 8 | 6 | 5 | 5 | 5 | 4 | 3 |
| Surg Alone | 13 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Surg + Chemo | 91 | 41 | 19 | 12 | 11 | 8 | 6 | 6 | 4 | 3 | 2 | 2 | 2 | 2 | 2 | 1 |
| Surg+RT | 4 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Surg + Chemo + RT | 18 | 11 | 7 | 7 | 7 | 6 | 4 | 4 | 3 | 3 | 2 | 2 | 2 | 2 | 1 | 1 |
| Surg + Chemo/RT + HDC | 19 | 14 | 9 | 5 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| Missing | 24 | 5 | 4 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

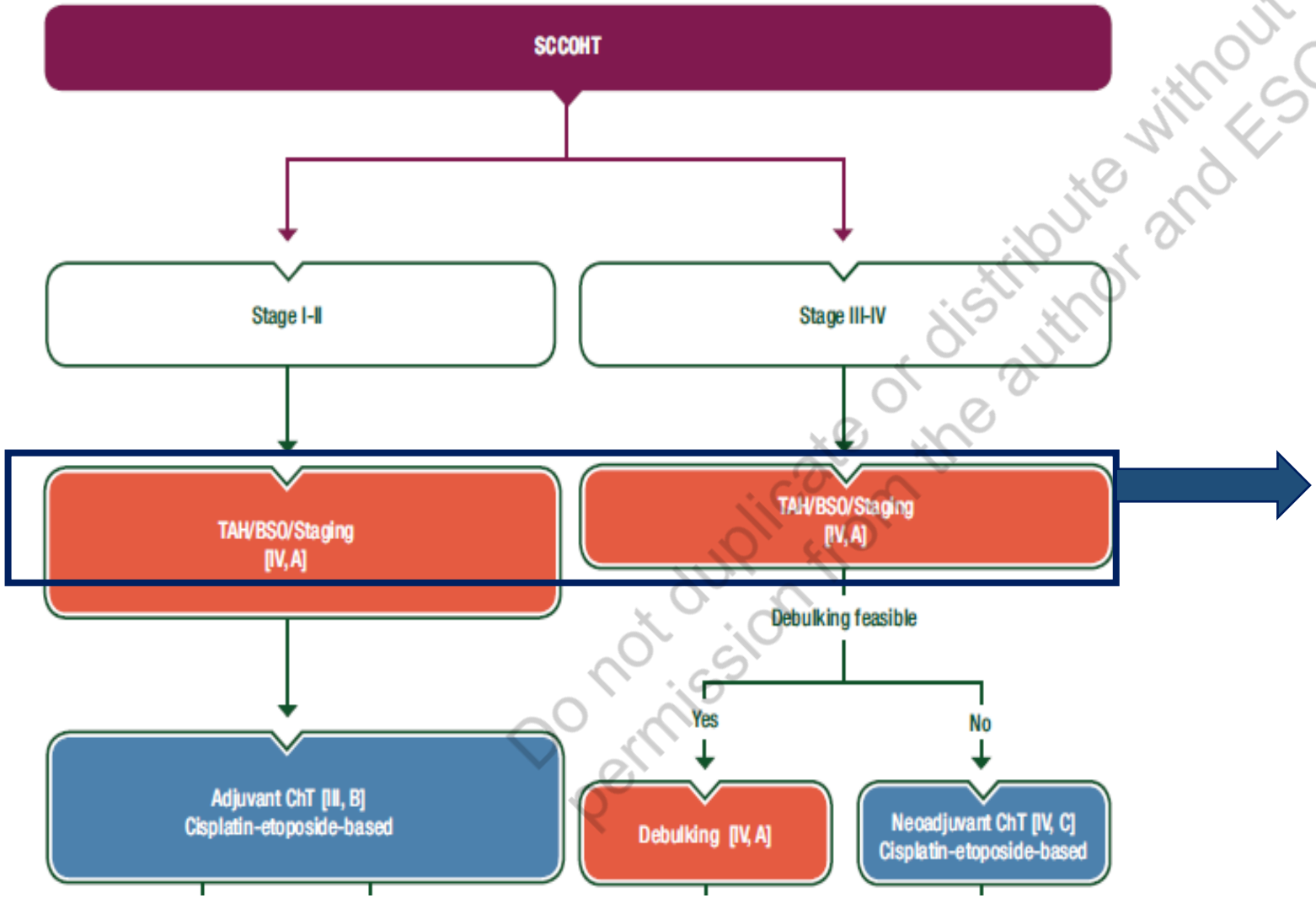
Best outcome obtained with surgery+chemo/RT+ HDCT (71% OS on 19 patients)

No advantage in adding RT to surgery + chemotherapy



*Witkowski L et al., Gynecol Oncol 2016*
*Ray Coquard I et al., ESMO Guidelines, Ann Oncol 2018*
*Tischkowitz M et al. Clin Cancer Res 2020*

# ESMO Guidelines - Surgery

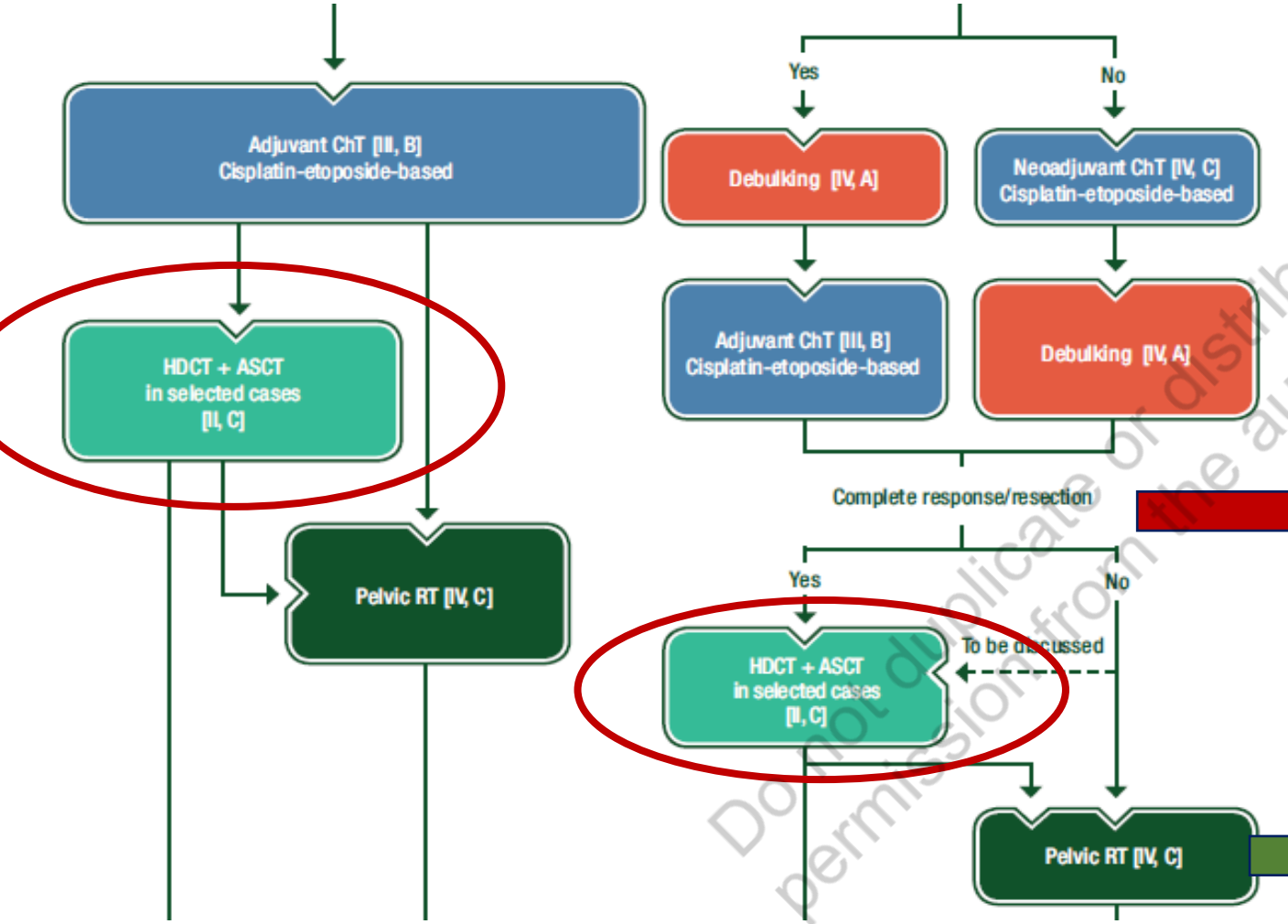



BSO + hysterectomy+ peritoneal and nodal staging surgery



*Ray Coquard I, et al. ESMO Guidelines, Ann Oncol 2018*

# ESMO Guidelines - Adjuvant treatment




Cisplatin – etoposide combination regimens (EP, BEP, VPCBAE, PAVEP..)

HDCT + ASCT in case of complete response as consolidation treatment

RT in case of residual disease after chemotherapy



*Ray Coquard I, et al. ESMO Guidelines, Ann Oncol 2018*
*Pautier P et al. Ann Oncol 2017*
*Witkowski L et al. Gynecol Oncol 2016*

# Treatment of recurrent disease

Prolonged remissions not achievable with second line chemotherapy

| |
|---|
| **Cyclophosphamide, doxorubicin, vincristine** |
| **Carboplatin paclitaxel (also dose dense)** |
| **Topotecan** |
| **Phase I trials** |

**Oncologic Management: Recurrent Disease**

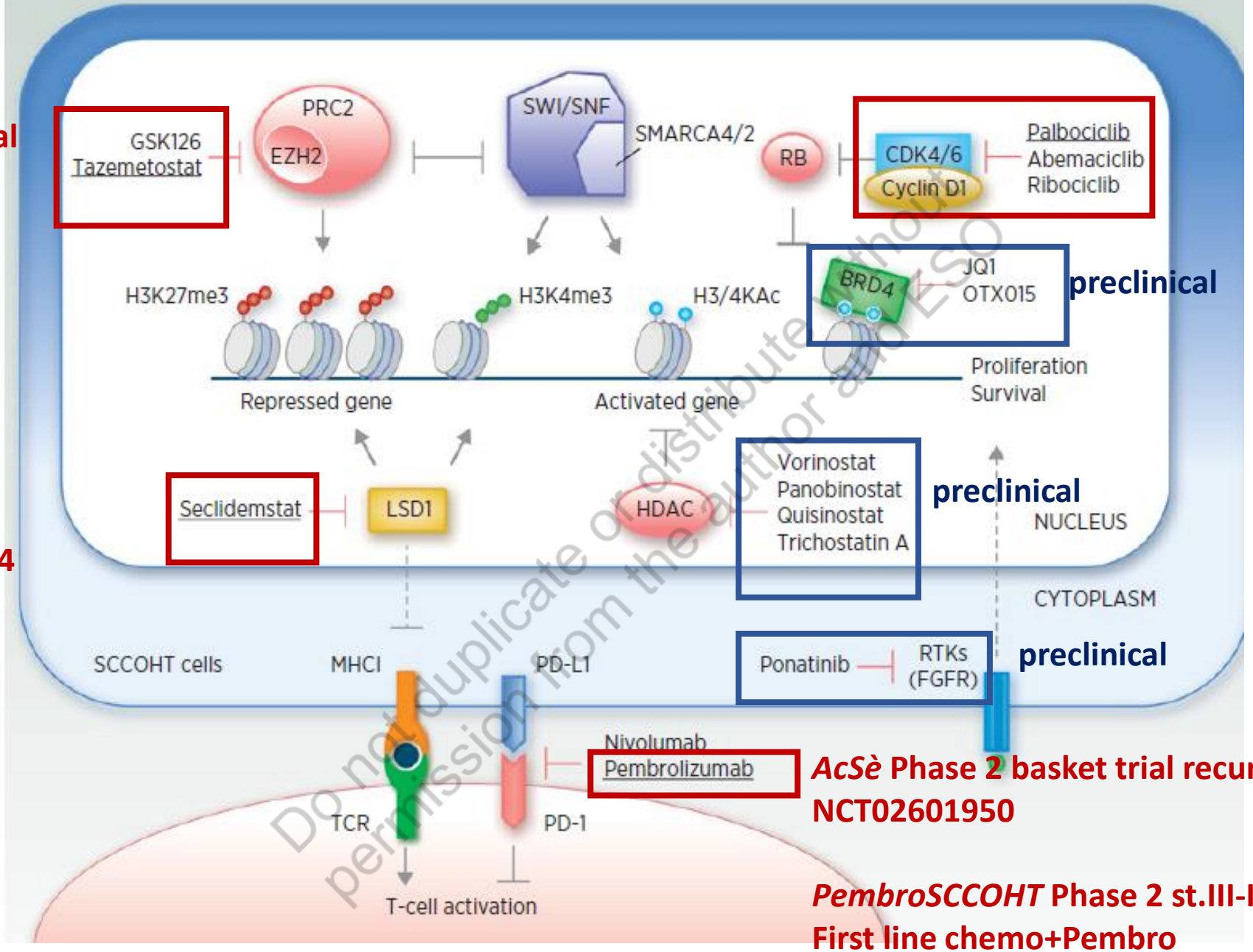
- Obtain biopsy as clinically indicated and/or to help with ongoing translational research[a].
- Enroll in clinical trial, if available (see Table 2).
- Consider radiotherapy if disease field allows.
- Consider additional chemotherapy with cisplatin and etoposide combination regimens if disease-free interval > 6 months.
- Alternative chemotherapy regimens (cyclophosphamide, doxorubicin, vincristine; or carboplatin, paclitaxel; or topotecan; or similar).
- Consider secondary surgical cytoreduction if disease can be completely resected and disease-free interval > 12 months[b].
- Consider off-label immune checkpoint blockade treatment after radiotherapy based on drug availability (69).
- Consult with members of the ISC regarding off-label drug use based on unpublished data.



*Ray Coquard I, et al. ESMO Guidelines, Ann Oncol 2018*
*Tischkowitz M et al. Clin Cancer Res 2020*

**Phase 2 basket trial**
**NCT02601950**

**Phase 2 trial**
**NCT03297606**
**(palbociclib)**




**Phase 1 trial**
**NCT03895684**

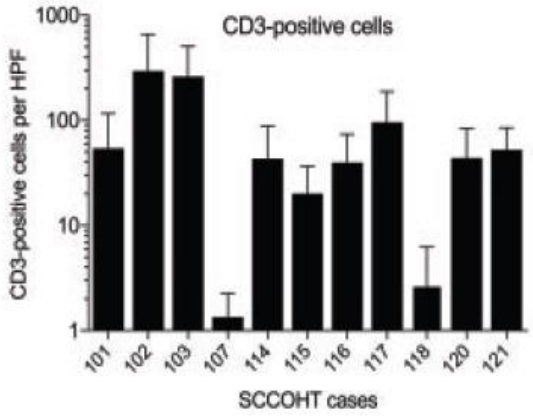
***AcSè* Phase 2 basket trial recurrent rare OC**
**NCT02601950**

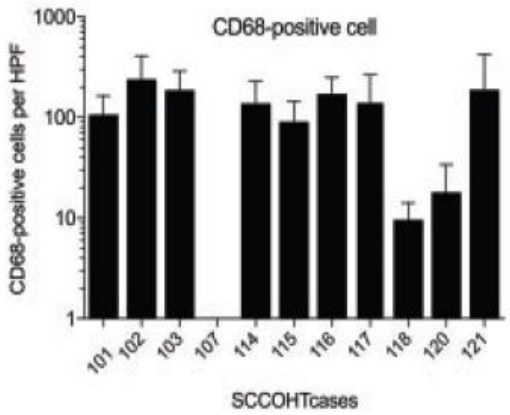
***PembroSCCOHT* Phase 2 st.III-IV**
**First line chemo+Pembro**

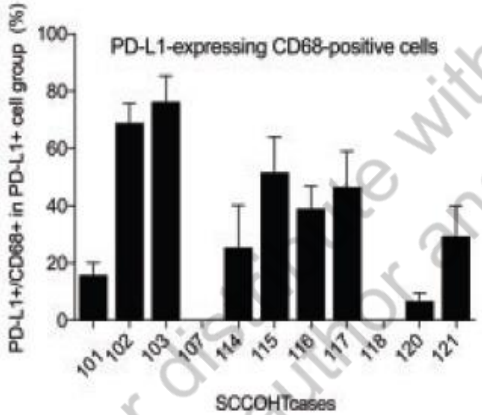


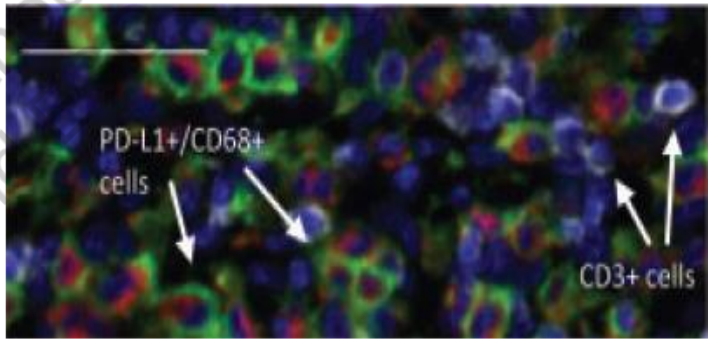
*Tischkowitz M et al. Clin Cancer Res 2020*

# Immune checkpoint inhibitors in SCCOH






***AcSè* - NCT03012620**

**Phase 2 basket trial with Pembrolizumab in recurrent rare OC**

***PembroSCCOHT* - NCT04602377–**

**Phase 2 trial of chemotherapy + Pembrolizumab for stage III-IV SCCOH**

*Jelinic P et al., J Natl Cancer Inst 2018*

# SCCOHT-Conclusions

- Rare tumors, with aggressive disease course and poor prognosis
- Referral to reference centers is mandatory – expert gyn pathological review at diagnosis
- Multimodality treatment recommended
- Mainstay of treatment is cytoreductive surgery followed by platinum/etoposide based chemotherapy
- Role of radioterapy still unclear
- High dose chemotherapy+ASCT as consolidation may improve outcome after response to chemotherapy
- Promising approaches: Target therapies to SWI/SNF complex, immunotherapy (phase I-II trials)
- **Promotion of international collaborations for registries and future clinical research.**



*Ray Coquard I, et al. ESMO Guidelines, Ann Oncol 2018*

# Small cell carcinoma of the uterine cervix

# Pathology

WHO Classification of neuroendocrine tumors (NETs) of the uterine cervix (1.4% of CC)

| | | |
|---|---|---|
| Uterine cervix | Neuroendocrine tumors | Carcinoid<br>Atypical carcinoid |
| | Neuroendocrine carcinoma | Small cell neuroendocrine carcinoma<br>Large cell neuroendocrine carcinoma |
| | | Adenocarcinoma/squamous cell carcinoma<br>Admixed with neuroendocrine carcinoma |

→ Most common: NET of small cell type (SCNET)



Differential diagnoses

- Lymphomas
- Squamous cell carcinoma of small cell type

*Colgan TJ et al, IARC press, 2014*
*Howitt BE, Curr Oncol Report 2017*

# Pathological diagnosis

GYNECOLOGIC CANCER INTERGROUP
An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

## SCCC
## Specific needs for histology diagnosis

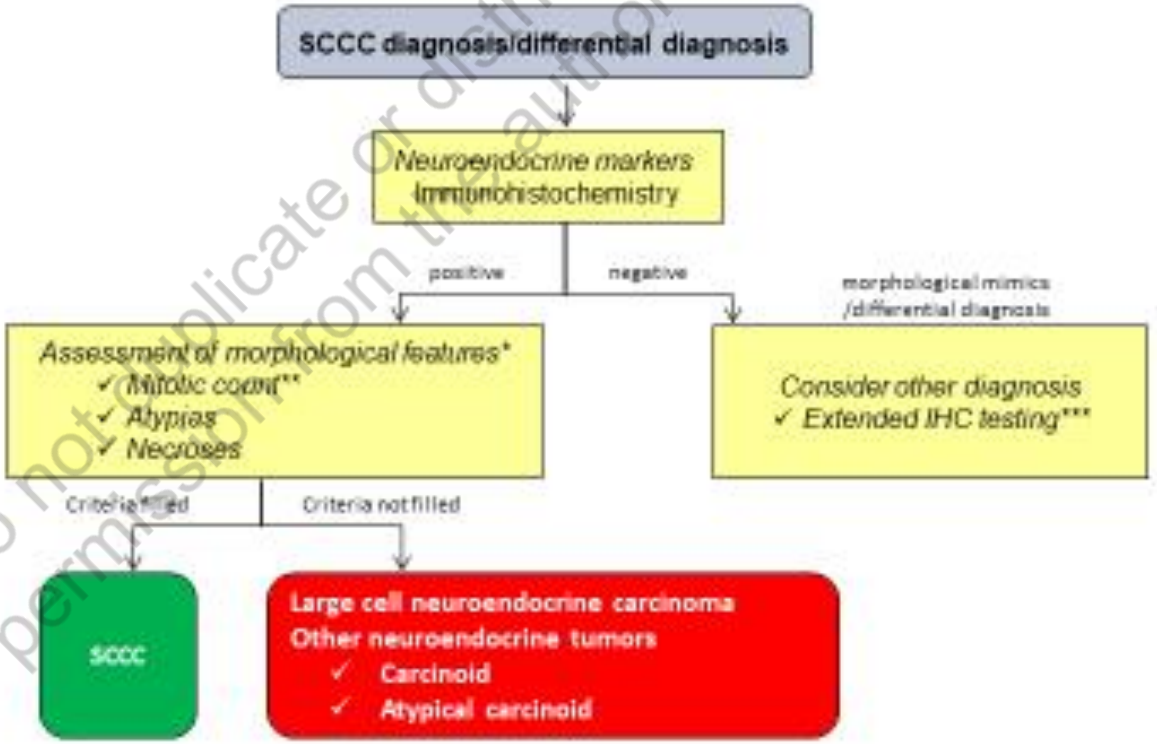
ESGO
European Society of Gynaecological Oncology



Specific IHC need to be done

Neuroendocrine markers

- ✓ Synaptophysin
- ✓ Chromogranin
- ✓ CD56 (low specificity)




*Exclude morphological mimics such as Ewing sarcoma / PNET; additional tests may be needed.
**Criteria for mitotic count are suggested (SCCC > 10 mitoses / 50 HPF; or > 10 mitoses / 10 HPF) but not exactly established
***Negativity of neuroendocrinne markers is not excluding SCCC; consider complex results of IHC antibodies panel

*Solheim O et al. GCIG guidelines 2021, presented at ESGO 2021*

# IHC profile

| | SCNET | Squamous cell carcinoma | Endocervical adenocarcinoma |
|---|---|---|---|
| **Pankeratin** | + | +++ | +++ |
| **CK7** | -/+ | -/+ | +++ |
| **Neuroendocrine markers** | 30-50%+ | Usually - | Usually - |
| **P16** | +++ | +++ | +++ |
| **TTF1** | +/- | - | - |
| **P63** | -/+ | +++ | - |
| **CEA** | - | - | +++ |
| **ER-PR** | - | + | - |
| **HPV** | HPV 18(53%)>HPV 16 | HPV 16>18 (15%) | 18 (50%)>16 |



IHC expression of neuroendocrine markers not required for diagnosis

*Adapted from Satoh T et al, Int J Gynecol Cancer, 2014*

# Epidemiology SCNEC

| | Small cell carcinoma | Squamous cell carcinoma | Endocervical adenocarcinoma |
|---|---|---|---|
| Incidence, % cases | 1-5% | 75% | 20-25% |
| Mean age at diagnosis, years | 49<br>(14-78) | 52 | 46 |
| Behaviour | Aggressive | | |
| Disease spread | Lymph nodes 50%<br><br>Distant metastases<br>(lung, liver, bone, brain) | Lymph nodes 15-50%<br><br>Pelvic recurrences<br>Distant metastases<br>rare, lung 6% | Lymph nodes 20%<br><br>Ovary 5%<br>Lymph nodes, adrenal glands, lung |



*Adapted from Satoh T et al, Int J Gynecol Cancer, 2014*

# FIGO staging
# for carcinoma of the cervix

**Stage I:** The cancer has spread from the cervix lining into the deeper tissue but is still just found in the uterus. It has not spread to other parts of the body. This stage may be divided into smaller groups to describe the cancer in more detail (see below).
**Stage IA:** The cancer is diagnosed only by viewing cervical tissue or cells under a microscope. Imaging tests or evaluation of tissue samples can also be used to determine tumor size.
- **Stage IA1:** There is a cancerous area of less than 3 millimeters (mm) in depth.
- **Stage IA2:** There is a cancerous area 3 mm to less than 5 mm in depth.

**Stage IB:** In this stage, the tumor is larger but still only confined to the cervix. There is no distant spread.
- **Stage IB1:** The tumor 5 mm or more in depth and less than 2 centimeters (cm) wide. A centimeter is roughly equal to the width of a standard pen or pencil.
- **Stage IB2:** The tumor is 2 cm or more in depth and less than 4 cm wide.
- **Stage IB3:** The tumor is 4 cm or more in width.

**Stage II:** The cancer has spread beyond the uterus to nearby areas, such as the vagina or tissue near the cervix, but it is still inside the pelvic area. It has not spread to other parts of the body. This stage may be divided into smaller groups to describe the cancer in more detail (see below).
**Stage IIA:** The tumor is limited to the upper two-thirds of the vagina. It has not spread to the tissue next to the cervix, which is called the parametrial area.
- **Stage IIA1:** The tumor is less than 4 cm wide.
- **Stage IIA2:** The tumor is 4 cm or more in width.

**Stage IIB:** The tumor has spread to the parametrial area. The tumor does not reach the pelvic wall.

**Stage III:** The tumor involves the lower third of the vagina, and/or has spread to the pelvic wall, and/or causes swelling of the kidney, called hydronephrosis, or stops a kidney from functioning, and/or involves regional lymph nodes. There is no distant spread.
**Stage IIIA:** The tumor involves the lower third of the vagina, but it has not grown into the pelvic wall.
**Stage IIIB:** The tumor has grown into the pelvic wall and/or affects a kidney.
**Stage IIIC:** The tumor involves regional lymph nodes. This can be detected using imaging tests or pathology. Adding a lowercase "r" indicates imaging tests were used to confirm lymph node involvement. A lowercase "p" indicates pathology
- **Stage IIIC1:** The cancer has spread to lymph nodes in the pelvis.
- **Stage IIIC2:** The cancer has spread to para-aortic lymph nodes. These lymph nodes are found in the abdomen near the base of the spine and near the aorta, a major artery that runs from the heart to the abdomen.

**Stage IVA:** The cancer has spread to the bladder or rectum, but it has not spread to other parts of the body.
**Stage IVB:** The cancer has spread to other parts of the body.

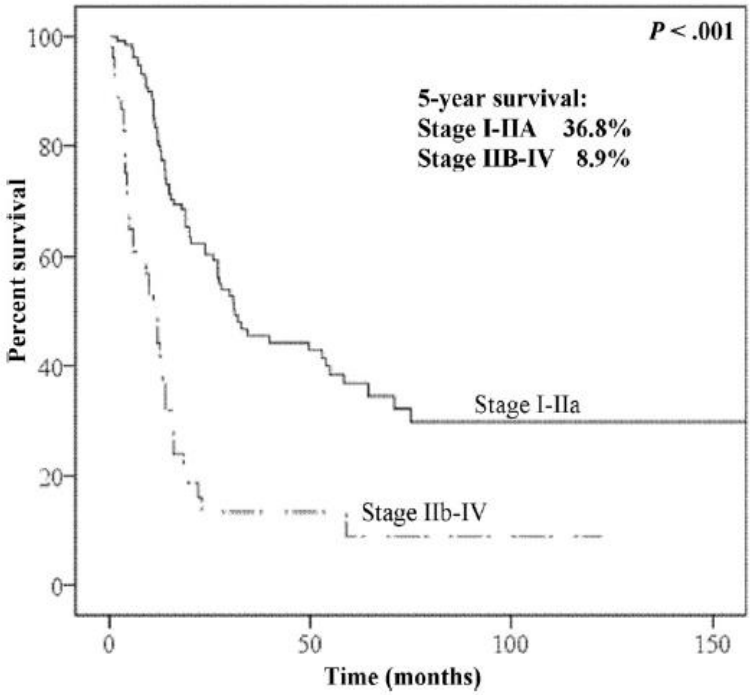
***Source:** Bhatla N, et al. Revised FIGO staging for carcinoma of the cervix uteri.* Int J Gynecol Obstet *2019; 1–7.*

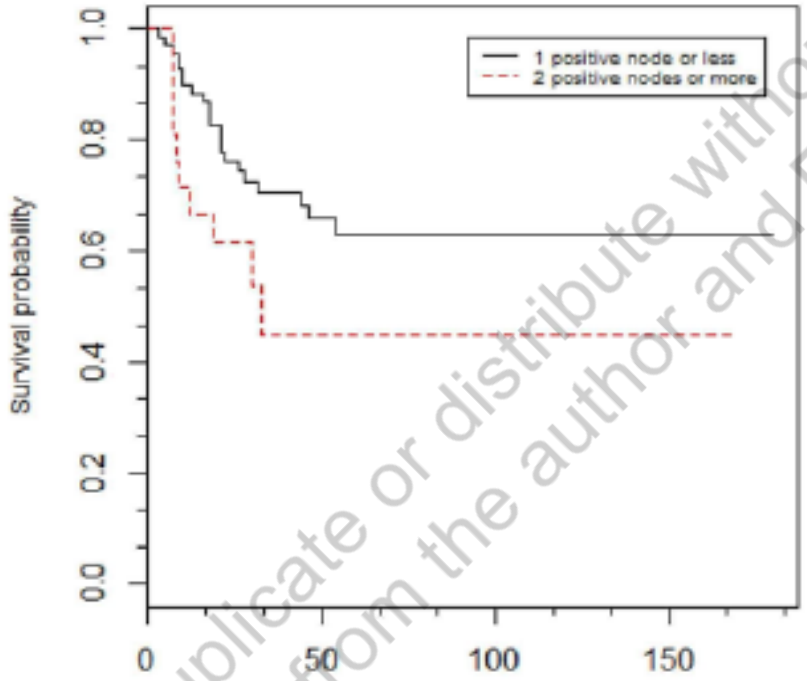




*Solheim O et al. GCIG guidelines 2021, presented at ESGO 2021*

# Prognosis






PROGNOSTIC FACTORS

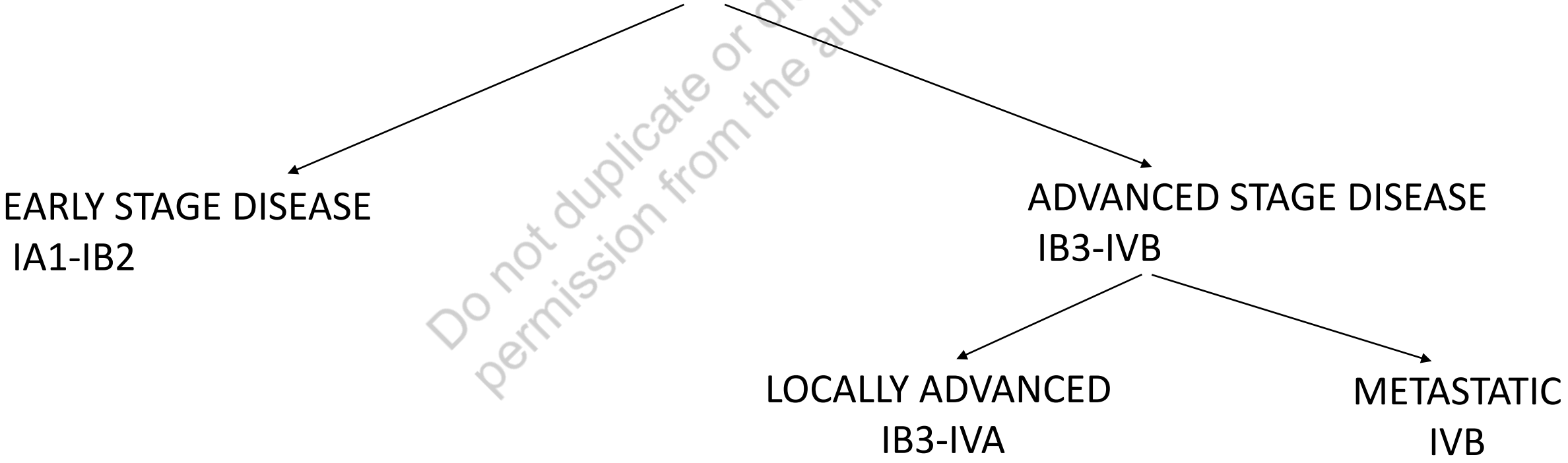
- **STAGE**
- **Pure small cell histology**
- Tumor size
- **LN status**
- **Age**
- LVSI
- Depth of invasion
- Margin status

5 y OS
- all stages 20-30%
- Stage I-II 30-50%
- Stage III-IV 0-10%

*Solheim O et al, GCIG guidelines, ESGO 2021*
*Cohen GJ et al. Am J Obstet Gynecol 2010*
*Li J. Et al, Int J Gynecol Cancer 2020*
*Gadducci et al, Gynecol Oncol 2017*

# Clinical staging

1.Physical examination
2. Imaging - pelvic MRI/ gyn US
- PET/CT – WB MRI + CT chest , Brain MRI if clinically indicated
3. Blood hem+chemistry



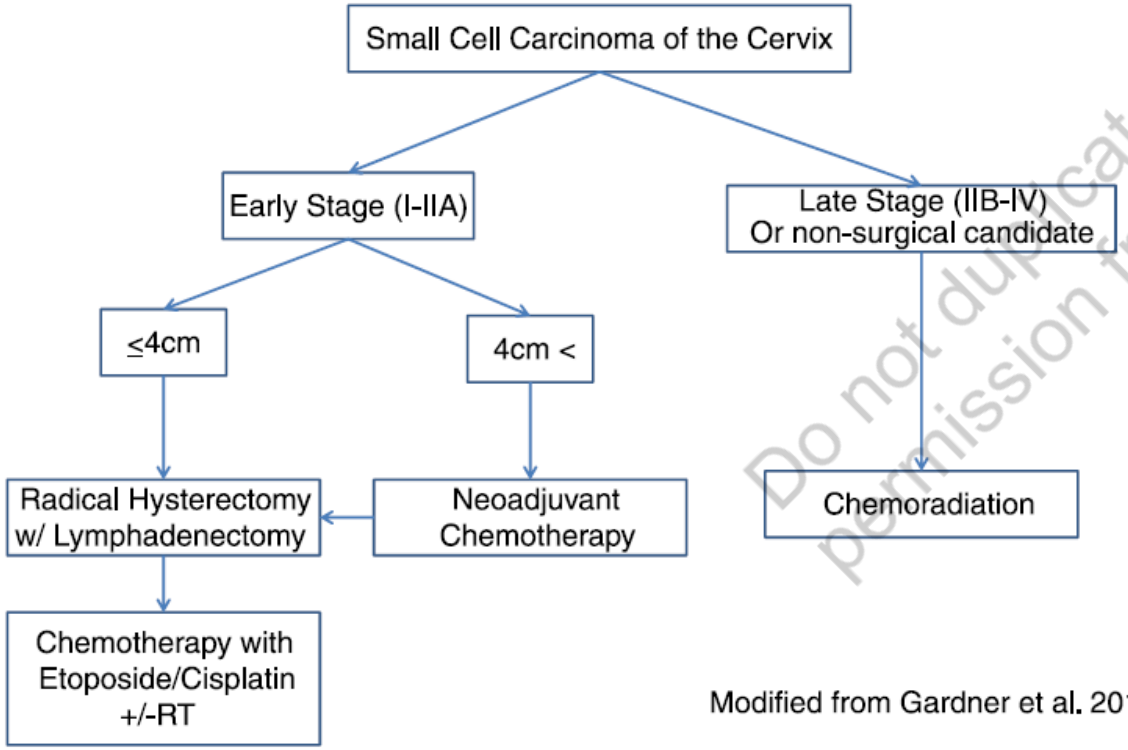



*Solheim O et al. GCIG guidelines 2021, presented at ESGO 2021*

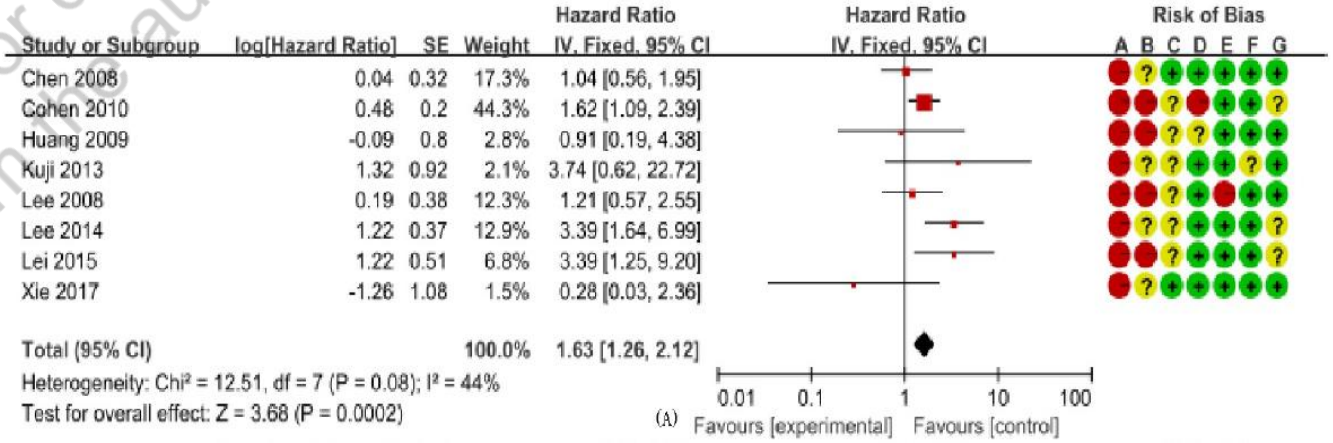
# Treatment

Lack of prospective studies – treatment based on retrospective case series with heterogeneous management and on management of lung SCNEC

MULTIMODALITY TREATMENT RECOMMENDED even in early stage disease

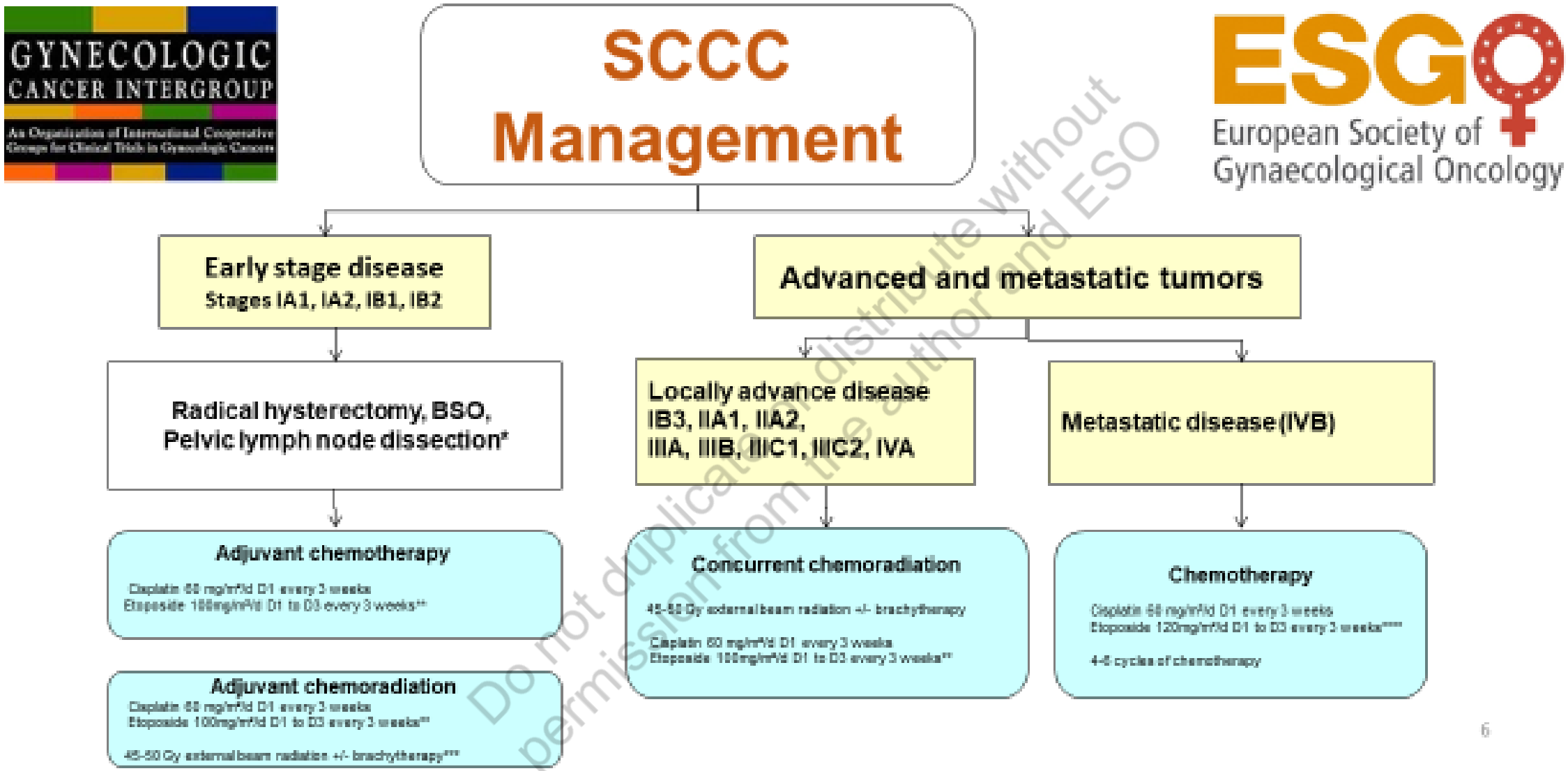



Modified from Gardner et al. 2011






*Satoh T et al, GCIG guidelines, 2014*








* Ovarian preservation and transposition can be considered in stage I premenopausal patients

** If possible six cycles of chemotherapy, with a minimum of five cycles total; consider Carboplatin/Etoposide if Creatinine clearance <60 ml/min

*** Optional

**** Etoposide 100mg/m2/d for those who are getting XRT or plan XRT

*Solheim O et al. GCIG guidelines 2021, presented at ESGO 2021*

# Chemotherapy regimens

**Table 5**
Chemotherapy regimens used for small cell neuroendocrine carcinoma of the uterine cervix.

| Author ref. | Settings | CT regimen |
|---|---|---|
| Boruta [33] | Adjuvant CT after surgery (N: 34) | PE (N: 15); VAC (N: 7); VAC/PE (N: 2); others (N: 10) |
| Chang [38] | Adjuvant CT after surgery (N: 23) | VAC/PE (N: 14); PVB (N: 8); others (N: 1) |
| Viswanathan [39] | NACT to RT (N: 8) | PAE (N: 7); PE (N: 1) |
| | CT/RT (n. 2) | P (N: 1); P-FU (N: 1) |
| | Adjuvant CT after surgery (N: 4) | PAE (N: 4) |
| Zivanovic [40] | Adjuvant CT after surgery or CT/RT (N: 6) | PE (N: 5); CE (N: 1) |
| Nagao [63][a] | Adjuvant CT after surgery (N: 9) | PI (N: 8); CP (n: 1) |
| | Adjuvant CT/RT after surgery (N: 7) | Nedaplatin (N: 6); P (N: 1) |
| Futagami [49] | Adjuvant concurrent CT/RT after surgery followed by adjuvant CT | Nedaplatin + PE |
| Bermúdez [50] | NACT (N: 13) | PVB (N: 13) |
| Nasu [48] | NACT to surgery followed by adjuvant CT | PI (N: 1) |
| Dongol [41] | NACT to surgery (N: 3) | PE (N: 1); PVB (N: 1); carboplatin-based CT (N: 1)[b] |
| | Adjuvant CT after surgery (N: 4) | PE (N: 2); PVB (N: 1); CP (N: 1) |
| Lewandowski [61] | NACT to surgery (N: 2) | PAE (N: 2) |
| | Adjuvant CT (N: 1) | PAE |
| | CT for metastatic disease (N: 1) | PAE |
| Cohen [64] | NACT or adjuvant CT or CT/RT (N: 81) | PE (N: 42); other P–based CT (N: 21); P (N: 6); others (N: 12) |
| Hoskins [37] | CT/RT (N: 31) | PE (N: 17); CP (N: 14) |
| Wang [42] | NACT or adjuvant CT or CT/RT (N: 144) | PE (N: 70); other platinum-based CT (N: 54); others (N: 20) |



<u>Most used:</u>

EP

Cisplatin 60 mg/mq d1

Etoposide 80-100 mg/mq d1,2,3 q 21/28d

<u>Others:</u>

Carboplatin/cisplatin + paclitaxel

Vincristine, cisplatin, bleomycin

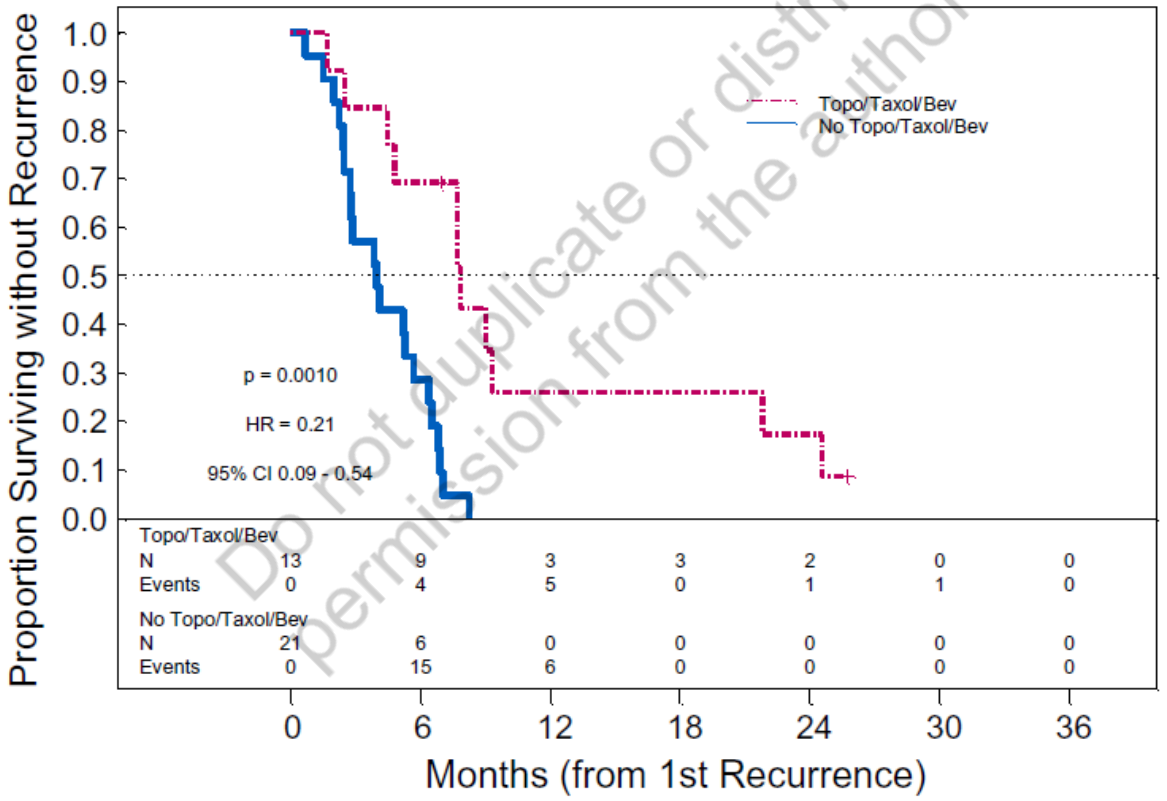
*Satoh T et al, GCIG guidelines, 2014*

# Recurrent disease

## Combination therapy with topotecan, paclitaxel, and bevacizumab improves progression-free survival in recurrent small cell neuroendocrine carcinoma of the cervix

M. Frumovitz [a,*], M.F. Munsell [b], J.K. Burzawa [a], L.A. Byers [c], P. Ramalingam [d], J. Brown [e], R.L. Coleman [a]

| |
|---|
| Topo |
| Pacli |
| Doce |
| Irino |





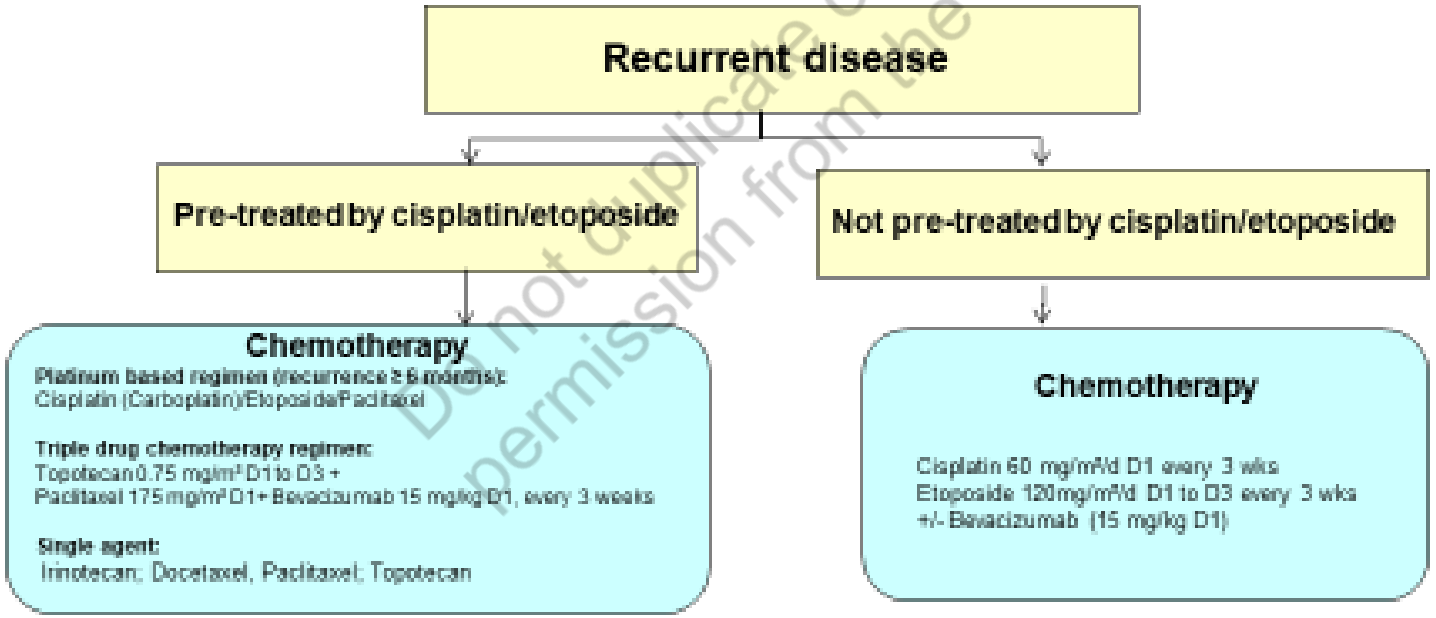

*Frumovitz etl a. Gynecol Oncol 2017*

# Treatment of recurrent disease – GCIG guidelines

## High-grade neuroendocrine cervical carcinoma
## First recurrence

Clinical staging:

Physical exam and symptoms
Local staging: pelvic MRI or expert ultrasound to assess tumor size, parametrial, and nodal disease
Distant staging: PET/CT scan or WB MRI or CT scan of chest, abdomen and pelvis (if PET or MRI is not available)
MRI of the brain
Blood counts and chemistries to assess critical organ function, including renal and hepatic function






*Solheim O et al. GCIG guidelines 2021, presented at ESGO 2021*

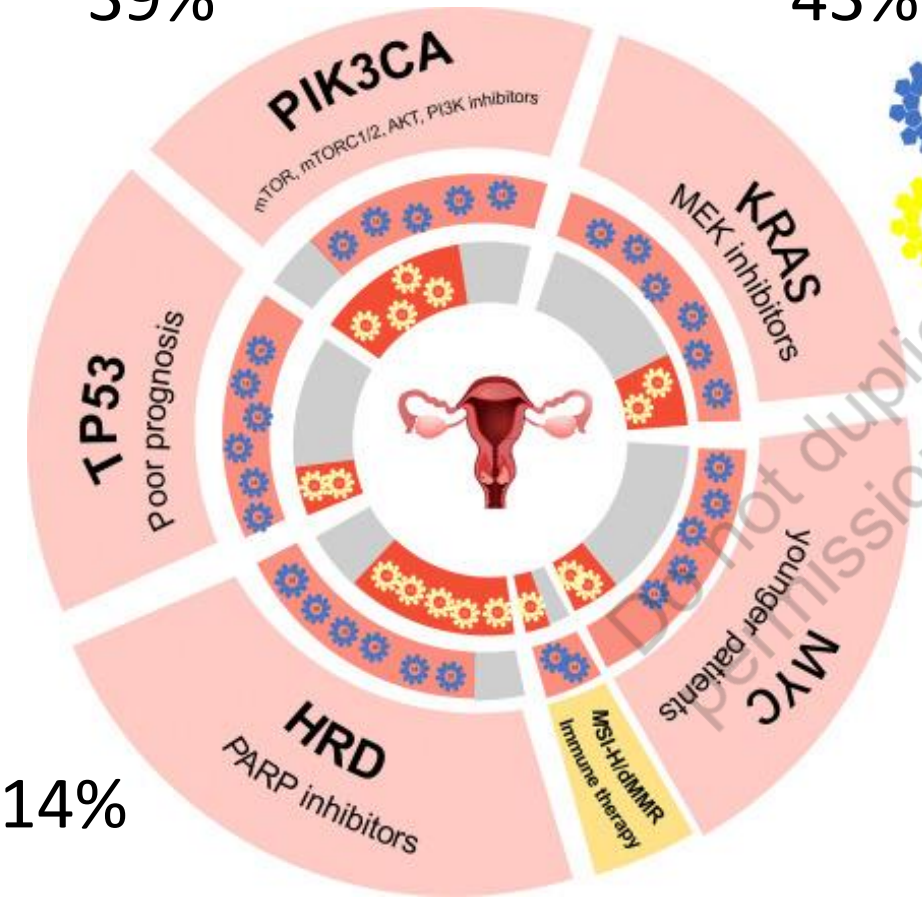
# Future perspectives

The next generation sequencing of cancer-related genes in small cell neuroendocrine carcinoma of the cervix

Xuan Pei [a,b,1], Libing Xiang [c,1], Wei Chen [a,b,d], Wei Jiang [a,b], Lina Yin [a,b], Xuxia Shen [b,e], Xiaoyan Zhou [b,e], Huijuan Yang [a,b,*]

39%

43%

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Metastatic small cell neuroendocrine carcinoma of the cervix treated with the PD-1 inhibitor, nivolumab: a case report

Sarah E. Paraghamian, Teresa C. Longoria and Ramez N. Eskander*



*Pei X et al, Gynecol Oncol 2021*

*Paraghamian et al, Gyn Oncol Res Pract 2017*

# SCNET Conclusions

- Rare tumors with agressive disease course and poor prognosis
- Multimodality treatment recommended: surgery + EP based chemo/radiotherapy
- Recurrent disease: single agent chemotherapy, topotecan/paclitaxel/bevacizumab
- Promising approaches: Immunotherapy, MEK-inhibitors, PIK3CA inhibitors need further investigation
- **International collaborations for clinical research**