



Chemotherapy in Children, Teenagers, and Young Adults Gynecologic Cancer Patient

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DECLARATION OF INTERESTS

Nothing to declare

Contents

- ✓ Definition
- ✓ Epidemiology
- ✓ Malignant germ cell tumor in Children and AYAs
- ✓ Gonadotoxicity of chemotherapy:
 - Primary Ovarian Insufficiency & Fertility preservation
- ✓ Late effects of treatment in survivors

Children/Teenagers/Young Adults - Definition

American Cancer Society/National Cancer Institute

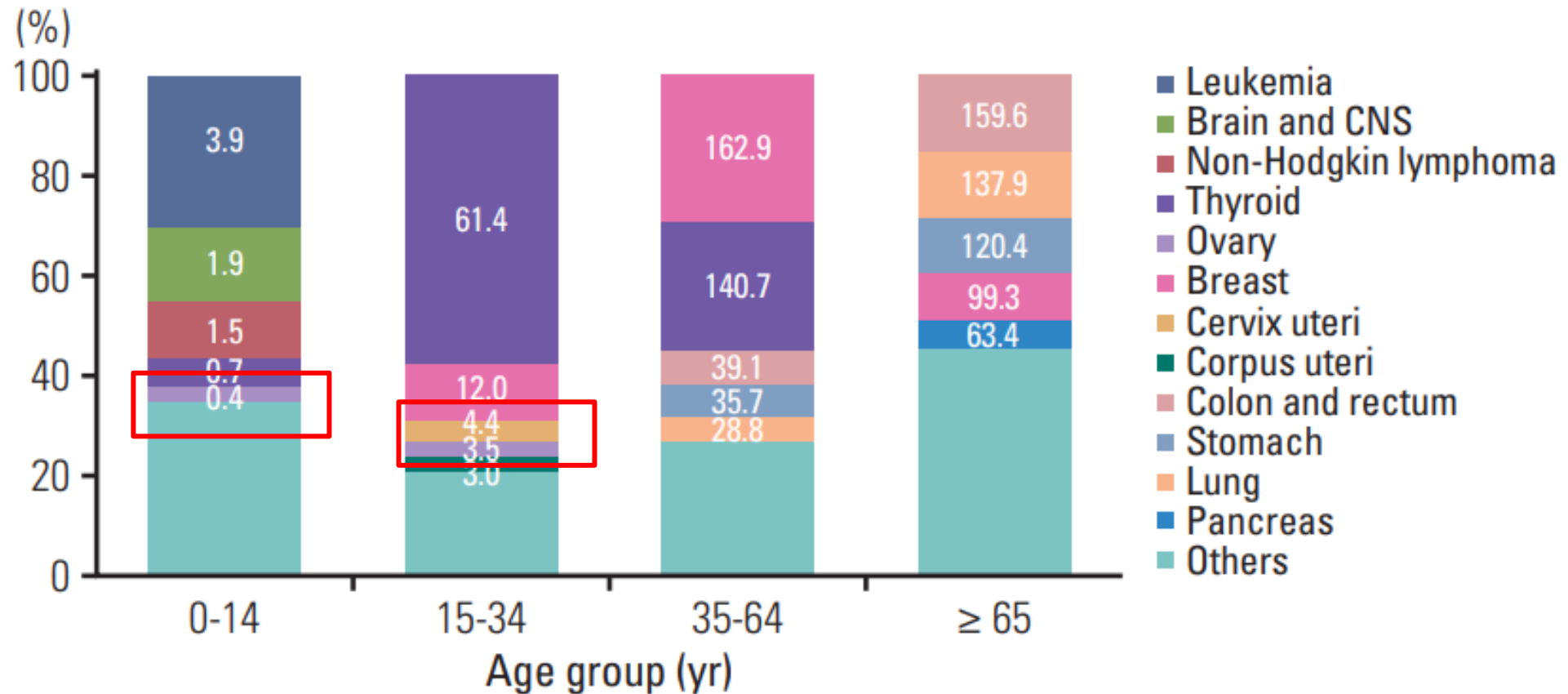
- Children: Birth-14
- Adolescents: 15-19
- Young Adults: 20-39

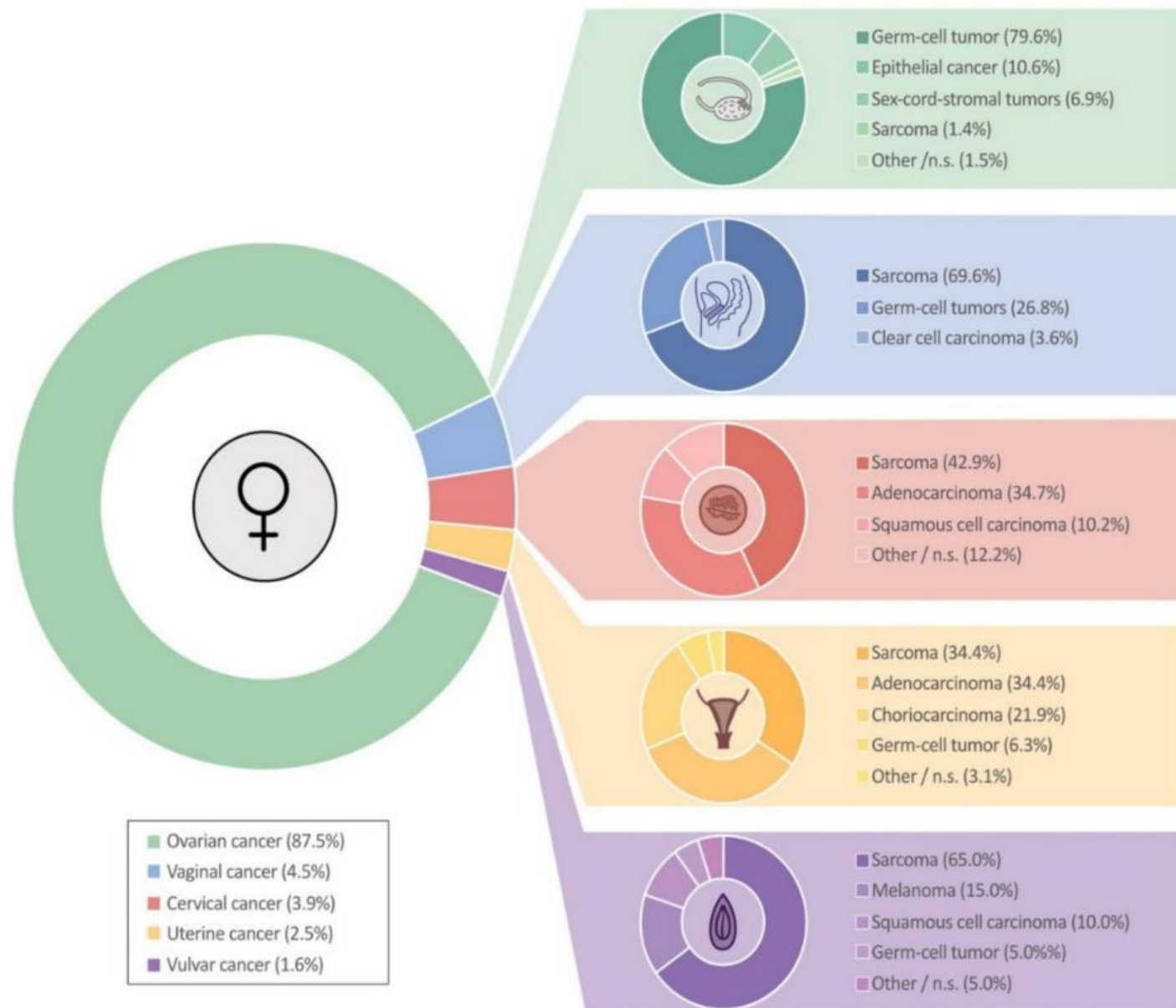
Regional Variations

Groups	Age range	
UK	13-24	Teenagers/young adults (TYA)
Australia	15-24	Adolescents/young adults (AYA)
USA (NCI, NCCN)	15-39	Adolescents/young adults (AYA)
Eurocare	15-24	Adolescents/young adults (AYA)
Canada	15-29	Adolescents/young adults (AYA)
Korea	0-19	소아· 청소년암

/ The five common sites of cancer incidence by age group and sex for 2019 in Korea (Women)

Numbers in parentheses are age-specific incidence rates per 100,000





Distribution of gynecologic malignancies according to histology (SEER-18 population)



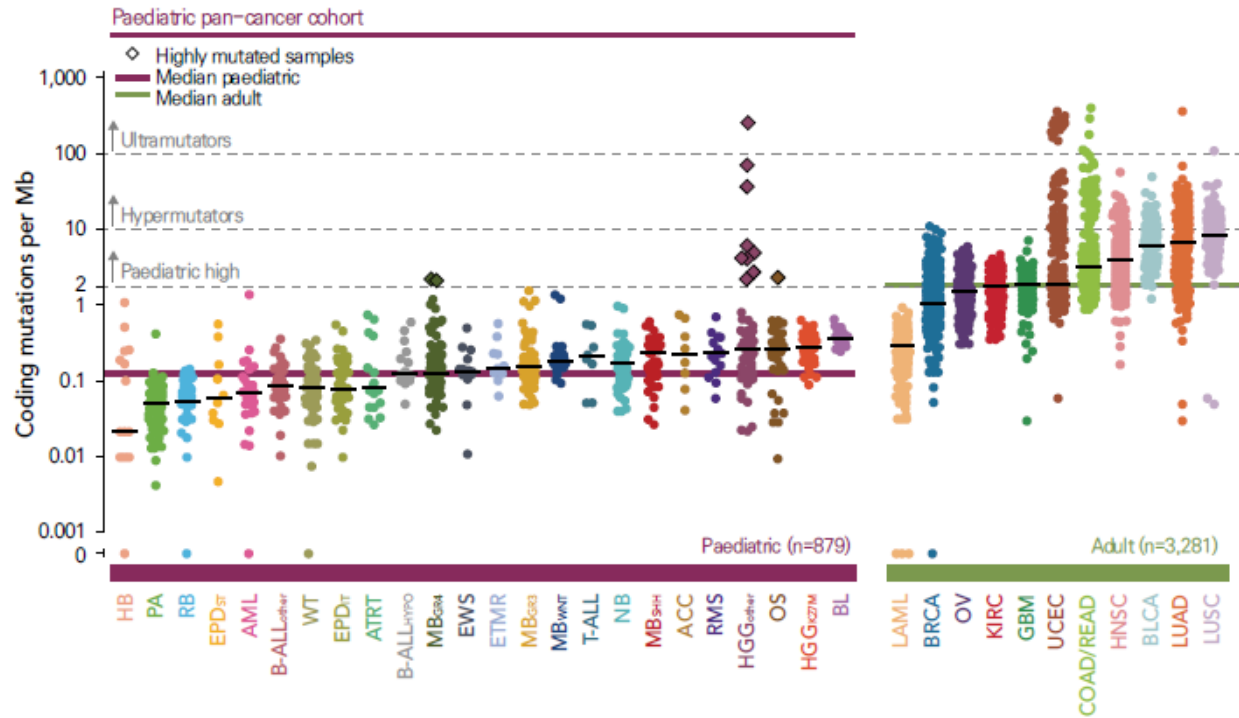
제 7 장 Special Issue 소아청소년암



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	소아기	청소년 및 청년기		
연령	0-14세	15-19세	20-24세	25-29세
		갑상선암이 가장 높은 비율 차지		
주요 암종분포	백혈병, 골수증식질환, 골수형성 이상증후군 (30.5%) 신경모세포종 및 기타 말초신경 세포종양 (9.7%) 연조직 및 기타 육종 (8.6%) 생식세포종양 (8.2%) 상피성 신생물 (7.7%) 악성골종양 (5.7%)	(갑상선암 제외) 백혈병 (22.2%) 림프종 (15.0%) 생식세포종양 (12.8%) 골연골종양(10.5%) 중추신경계종양 (9.3%)	(갑상선암 제외) 상피성암 (32%) 백혈병 (14.1%) 림프종 (14.2%) 중추신경계종양 (6.8%)	(갑상선암 제외) 상피성암 (55.7%) – 유 방암과 자궁경부암이 40% 차지 백혈병 (8.3%) 림프종 (8.8%) 중추신경계종양 (5.2%)
			상피성암 비중 점차 증가	상피성암이 대부분을 차지

성인암과 다른 소아청소년암 유전체의 특징



Molecular cancer types in paediatric pan-cancer cohort

- Hepatoblastoma (HB) (n=16)
- Piloicytic astrocytoma (PA) (n=105)
- Retinoblastoma (RB) (n=36)
- Ependymoma supratentorial (EPD_{ST}) (n=15)
- Acute myeloid leukaemia (AML) (n=30)
- B-cell acute lymphoblastic leukaemia, non-hypodiploid (B-ALL_{non}) (n=61)
- Wilms tumour (WT) (n=51)
- Ependymoma infratentorial (EPD_{IT}) (n=55)
- ATRT (n=19)
- B-cell acute lymphoblastic leukaemia, hypodiploid (B-ALL_{HYPO}) (n=20)
- Medulloblastoma Group 4 (MB_{GR4}) (n=107)
- Ewing's sarcoma (EWS) (n=24)
- ETMR (ETMR) (n=11)
- Medulloblastoma Group 3 (MB_{GR3}) (n=60)
- Medulloblastoma WNT (MB_{WNT}) (n=21)
- T-cell acute lymphoblastic leukaemia (T-ALL) (n=19)
- Neuroblastoma (NB) (n=59)
- Medulloblastoma SHH (MB_{SHH}) (n=42)
- Adrenocortical carcinoma (ACC) (n=8)
- Rhabdomyosarcoma (RMS) (n=21)
- High-grade glioma K27wt (HGG_{K27wt}) (n=67)
- Osteosarcoma (OS) (n=42)
- High-grade glioma K27M (HGG_{K27M}) (n=57)
- Burkitt's lymphoma (BL) (n=15)

Adult cancer types (TCGA)

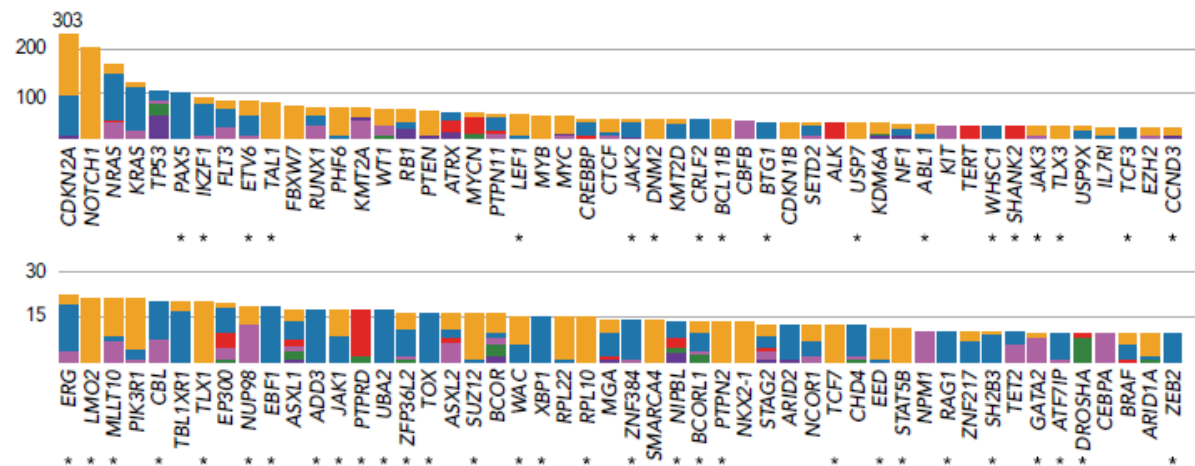
- Acute myeloid leukaemia (LAML)
- Breast adenocarcinoma (BRCA)
- Ovarian serous carcinoma (OV)
- Kidney renal clear cell carcinoma (KIRC)
- Glioblastoma (GBM)
- Uterine corpus endometrial carcinoma (UCEC)
- Colon/rectal carcinoma (COAD/READ)
- Head and neck squamous carcinoma (HNSC)
- Bladder urothelial carcinoma (BLCA)
- Lung adenocarcinoma (LUAD)
- Lung squamous cell carcinoma (LUSC)

출처: Gröbner SN, et al: The landscape of genomic alterations across childhood cancers. Nature. 2018 Mar 15;555(7696):321-32

- 성인암에 비해 체세포 돌연변이 빈도가 전반적으로 낮음.
- 암 발생 위험을 증가시키는 유전성 변이 (predisposition gene)가 발견됨. – 전체 환자의 7-10%
- 돌연변이 형태: fusion or copy number alteration > SNV
- CDKN2A를 포함한 암 유발유전자 분포도 성인암과 뚜렷한 차이를 보임.

소아청소년암의 driver gene 분포

■ B-ALL ■ T-ALL ■ AML ■ NBL ■ WT ■ OS



출처: Ma X, et al: Pan-cancer genome and transcriptome analyses of 1,699 paediatric leukaemias and solid tumors. Nature. 2018 Mar 15;555(7696):371-376



National Comprehensive
Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Adolescent and Young Adult (AYA) Oncology

Version 1.2026 — August 13, 2025

NCCN.org

NCCN recognizes the importance of clinical trials and encourages participation when applicable and available.
Trials should be designed to maximize inclusiveness and broad representative enrollment.

NCCN Guidelines for Patients® available at www.nccn.org/patients



REVIEW

Adolescents and young adults (AYA) with cancer: a position paper from the AYA Working Group of the European Society for Medical Oncology (ESMO) and the European Society for Paediatric Oncology (SIOPe)

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AYA ONCOLOGY

- Adolescents and young adults (AYA, 15–39 years) with cancer represent **a distinct population with unique biological, psychosocial, and behavioral characteristics**, and have experienced **slower improvements in survival** compared with younger children.
- Gynecologic malignancies in AYA are **rare but clinically complex**, most commonly involving the ovary, and require a **multidisciplinary and personalized model of care**.
- **Delayed diagnosis** is frequent due to low awareness, atypical symptom interpretation, and barriers to accessing specialized care.
- **Standard pediatric or adult oncology models alone are insufficient** to address the complex needs of AYA patients.
- **Enrollment in clinical trials remains low (5–34%)**, contributing to inferior outcomes; age-appropriate trial designs and improved access are critical.
- **Fertility preservation and reproductive health** are major concerns, necessitating early counseling and individualized oncofertility strategies.
- Long-term survivorship is often complicated by **ovarian insufficiency, reproductive dysfunction, and psychosocial sequelae**, highlighting the need for structured survivorship care plans.
- Optimal outcomes require **AYA-focused, multidisciplinary teams** integrating oncologic treatment, fertility preservation, psychological support, and survivorship planning.

Malignant germ



National
Comprehensive
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Network®

Printed by Na
NCCN
Malign

PATHOLOGIC DIAGNOSIS^a

Stage I
dysgerminomaⁱⁱ
or
Stage I, grade 1
immature
teratomaⁱⁱ

ADJUVANT TREATMENT

Observe
[Surveillance \(LCOC-B\)](#)

Any stage
embryonal
tumorⁱⁱ
or
Any stage
endodermal
sinus tumor (yolk
sac tumor)ⁱⁱ
or
Stage II–IV
dysgerminoma
or
Stage I, grade
2 or 3 or Stage
II–IV immature
teratoma
or
Any stage
nongestational
choriocarcinoma

Chemotherapyⁱⁱ

Imaging^p
as clinically
indicated:
eg, C/A/P
CT, chest
CT, A/P
MRI, PET/
CT, or PET/
MRI (skull
base to
mid-thigh)

clinical
response

[LCOC-14](#)

Residual
tumor on
radiographic
imaging;
markers
normal^{kk}

Persistently
elevated markers^{kk}
with definitive
residual disease

Biopsy
or
Consider
surgical
resection

or
Observe
([Surveillance](#)
[\[LCOC-B\]](#))

Necrotic
tissue

Follow path for complete
clinical response ([LCOC-14](#))

Benign
teratoma

C/A/P CT^p or MRI as
clinically indicated

Residual
malignancy

TIP (paclitaxel/ifosfamide/
cisplatin)
or
High-dose chemotherapyⁱⁱ +
hematopoietic cell transplant
(HCT) (strongly recommend
referral to tertiary care center for
potentially curative regimen)

[Surveillance](#)
[\(LCOC-B\)](#)

SYSTEMIC THERAPY REGIMENS^a MALIGNANT GERM CELL/SEX CORD-STROMAL TUMORS

MALIGNANT GERM CELL TUMORS^{a,b,c}

Primary
Therapy

Preferred Regimens

- BEP (bleomycin, etoposide, cisplatin)^d
 - ▶ Bleomycin 30 units IV per week plus etoposide 100 mg/m² IV daily on days 1–5 plus cisplatin 20 mg/m² IV daily on days 1–5; repeat every 21 days for 3 cycles for good risk (category 2B), or 4 cycles for poor risk.

Other Recommended Regimens

- None

Useful in Certain Circumstances

- Etoposide/carboplatin^{a,e} (for select patients with stage II–III resected dysgerminoma for whom minimizing toxicity is critical)
 - ▶ Carboplatin 400 mg/m² IV on day 1 plus etoposide 120 mg/m² IV on days 1, 2, and 3 every 28 days for 3 cycles.

Recurrence
Therapy

Preferred Regimens

(Potentially curative)

- High-dose chemotherapy^b
- TIP (paclitaxel, ifosfamide, cisplatin)

Other Recommended Regimens

(Palliative only)

- Etoposide/cisplatin (EP), if not previously used
- Docetaxel
- Docetaxel/carboplatin
- Etoposide (oral)
- Etoposide/ifosfamide/cisplatin (VIP)
- Gemcitabine/paclitaxel/oxaliplatin
- Gemcitabine/oxaliplatin
- Paclitaxel
- Paclitaxel/carboplatin
- Paclitaxel/gemcitabine
- Paclitaxel/ifosfamide
- Pembrolizumab (if microsatellite instability-high [MSI-H]/mismatch repair deficient [dMMR] or tumor mutational burden-high [TMB-H])
- VeIP (vinblastine, ifosfamide, cisplatin)
- VAC (vincristine, dactinomycin, cyclophosphamide)
- Supportive care (See [NCCN Supportive Care Guidelines](#))

Childhood Malignant Ovarian GCTs

Regimen	Bleomycin	Etoposide	Cisplatin	Carboplatin
Adult BEP (every 21 days) [11,19]	30 units/m ² , days 1, 8, 15 (maximum 30 units)	100 mg/m ² , days 1-5	20 mg/m ² , days 1-5	
Pediatric PEb (every 21 days) [3,13]	15 units/m ² , day 1 (maximum 30 units)	100 mg/m ² , days 1-5	20 mg/m ² , days 1-5	
Pediatric JEb (every 21-28 days) [14]	15 units/m ² , day 3 (maximum 30 units)	120 mg/m ² , days 1-3		600 mg/m ² or GFR-based dosing, day 2

BEP = bleomycin, etoposide, and cisplatin; GFR = glomerular filtration rate; JEb = carboplatin, etoposide, and bleomycin; PEb = cisplatin, etoposide, and bleomycin.

U.S.: ≤15 y (testicular), ≤21 y (ovarian/extragenadal)
[High risk] 6-year event-free survival 80.5%; OS 86.0%

UK: <16 y
[High risk] 5-year event-free survival 92%; OS 95%
Fewer otologic toxic effects and renal toxic effects than does the use of PEb.

Dysgerminoma		Stage I	Surgery → Observation
		Stage II-IV	Surgery + Chemotherapy (PEb)
Malignant Nongerminomatous Ovarian GCTs (Yolk sac tumor, Mixed GCTs)	Prepubertal females	Stage I (strict surgical staging)	Surgery → Observation
		Purported stage I / Stage II-IV	Surgery + Chemotherapy (PEb)
	Postpubertal females	Purported stage I / Stage II-IV	Surgery + Chemotherapy (BEP)
Initially Unresectable Tumors			Biopsy → Chemotherapy → Delayed Surgery

Late Effects of Treatment

	Cisplatin	Bleomycin	Long-Term Risks
Toxicities	<p>Ototoxicity High-frequency hearing loss affecting language development Can worsen over time, even years after treatment</p> <p>Nephrotoxicity ~15% irreversible decline in renal function Associated with increased cardiovascular and all-cause mortality</p> <p>Neurotoxicity Paraesthesia, more common in adults</p>	<p>Pulmonary toxicity in up to 50% of patients. Increased prevalence of restrictive lung disease 2.5-fold increased risk of pulmonary-related mortality</p>	<p>Twofold increased risk of cardiovascular disease.</p> <p>Increased risk of second malignancies. Risk increases ~1% per year without plateau. Younger age at treatment → higher lifetime cumulative risk.</p>

AYA Germ Cell Tumours - The AYA Gap in Care

- Some adolescents have historically been treated using paediatric protocols, leading to:
 - ✓ Lack of IGCCCG risk stratification
 - ✓ Missed opportunity for once-weekly bleomycin
 - ✓ Inability to receive lower cumulative cisplatin doses appropriate for good-risk disease
- Adolescent GCTs resemble adult disease more than childhood tumours
- Studies show worse outcomes in adolescents compared with both children and adults
- Adolescents often fall outside age eligibility criteria for both paediatric and adult trials
 - Under-representation in clinical trials and poorer outcomes
 - A clear example of the AYA gap in cancer care and research
- Moving Toward Age-Appropriate Care
 - ✓ Optimal outcomes require age-appropriate therapy in age-appropriate environments
 - ✓ Recognition of unique medical and psychosocial needs of AYA patients
 - ✓ National referral pathways (e.g., UK) now direct patients to specialist AYA cancer centres

Gonadotoxicity of Chemotherapy

- The degree of gonadotoxicity depends on the **mechanism of action, cumulative dose, and duration of treatment.**
- **Age dependency**; Gonadotoxicity is greater in older patients with reduced ovarian reserve
- Ovarian insufficiency can be transient or permanent.
- Depending on pubertal maturation level, peripubertal exposure can result in delayed or arrested puberty. Postpubertal exposure may lead to oligomenorrhea, amenorrhea, or compromised fertility

Risk	Regimen
High	Alkylating agents: ifosfamide, cyclophosphamide Busulfan, melphalan
Moderate	Platinum agents: cisplatin, carboplatin Taxanes, anthracyclines (doxorubicin)
Low (<20%)	Antimetabolites: gemcitabine, 5-fluorouracil Vincristine, methotrexate

Primary Ovarian Insufficiency (POI)

- Gonadotoxic cancer therapy can lead to loss of ovarian function
- Associated with:
 - Infertility,
 - Early menopausal symptoms (Dry eye syndrome, Osteopenia/osteoporosis → ↑ fracture risk, Early cardiovascular disease, Depression and anxiety, Early cognitive decline)
- Management
 - Most AYA with gynecologic cancer should receive **long-term hormone replacement therapy (HRT)**
 - Continue until the average age of natural menopause

Menstrual Suppression and Contraception

- Chemotherapy increases the risk of heavy menstrual bleeding (d/t thrombocytopenia)
- Sexually active AYA patients require effective contraception to prevent fetal malformations during chemo- or radiotherapy.
- Progestin-only methods; combined hormonal contraceptives; GnRH agonists
It is controversial whether menstrual suppression provides adequate protection for the ovaries.
- GnRH agonists may protect ovarian function; however, other fertility preservation modalities should still be considered and, if possible, pursued.

Phase III randomized POEMS trial (*ER-negative breast cancer*): Adding goserelin to chemotherapy significantly reduced premature ovarian failure and increased pregnancy and live birth rates.

ESMO 2020 guidelines: Recommend GnRH agonists as a standard option for ovarian function preservation in breast cancer and a reasonable option in other malignancies.

ASCO 2025 guidelines: Acknowledge improved ovarian function and pregnancy outcomes with GnRH agonists during chemotherapy, but include them only as a non-established option mainly supported by breast cancer data.

Ongoing ALTE-2131 trial: the role of GnRH agonists during chemotherapy for nonbreast malignancies

Fertility preservation

Individuals with Ovaries

- For patients who can **delay cancer treatment for approximately 3 weeks**, discuss **oocyte or embryo cryopreservation via immediate (or random start) controlled ovarian stimulation (COS)**.
- For patients who **cannot delay** treatment for oocyte or embryo cryopreservation and are at **high risk for impaired fertility**, discuss or refer the patient for consideration of **ovarian tissue cryopreservation**.
- For patients in whom the **radiation field will include the ovaries**, discuss **oophoropexy or transposition of the ovaries** out of the field of radiation.
- Discuss effects of treatment on gonadal hormone function during and after treatment. Some individuals face primary ovarian insufficiency and should be screened and treated by a specialist. Additionally, for individuals who did not undergo fertility preservation prior to treatment, some may still be eligible for fertility preservation after treatment is completed. After completion of treatment, screen or refer the patient to a specialist as appropriate.

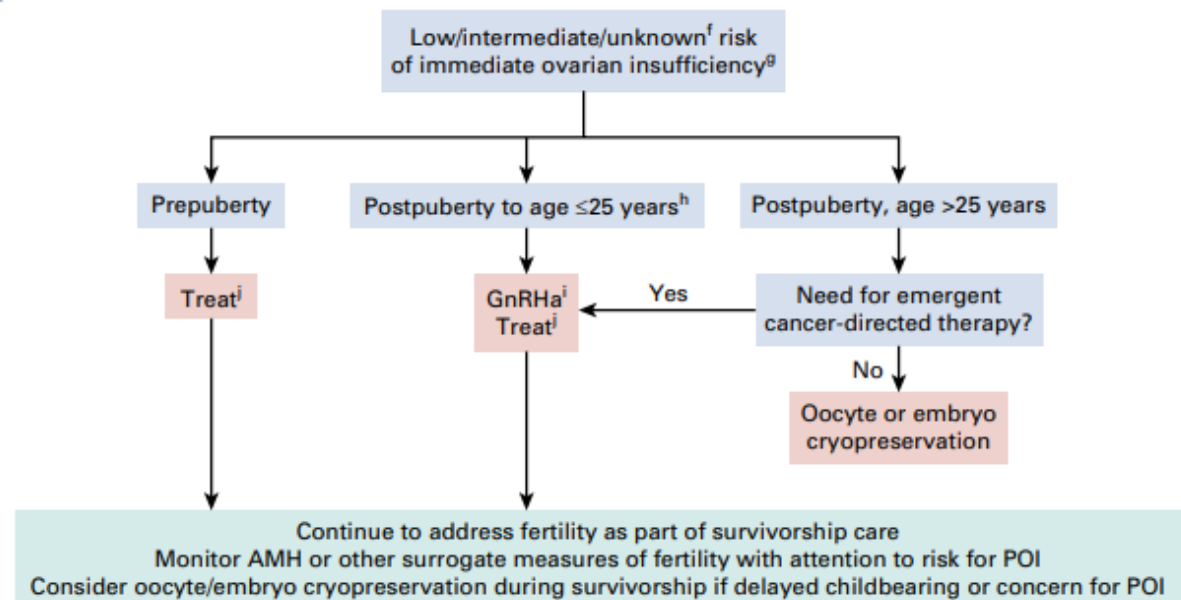
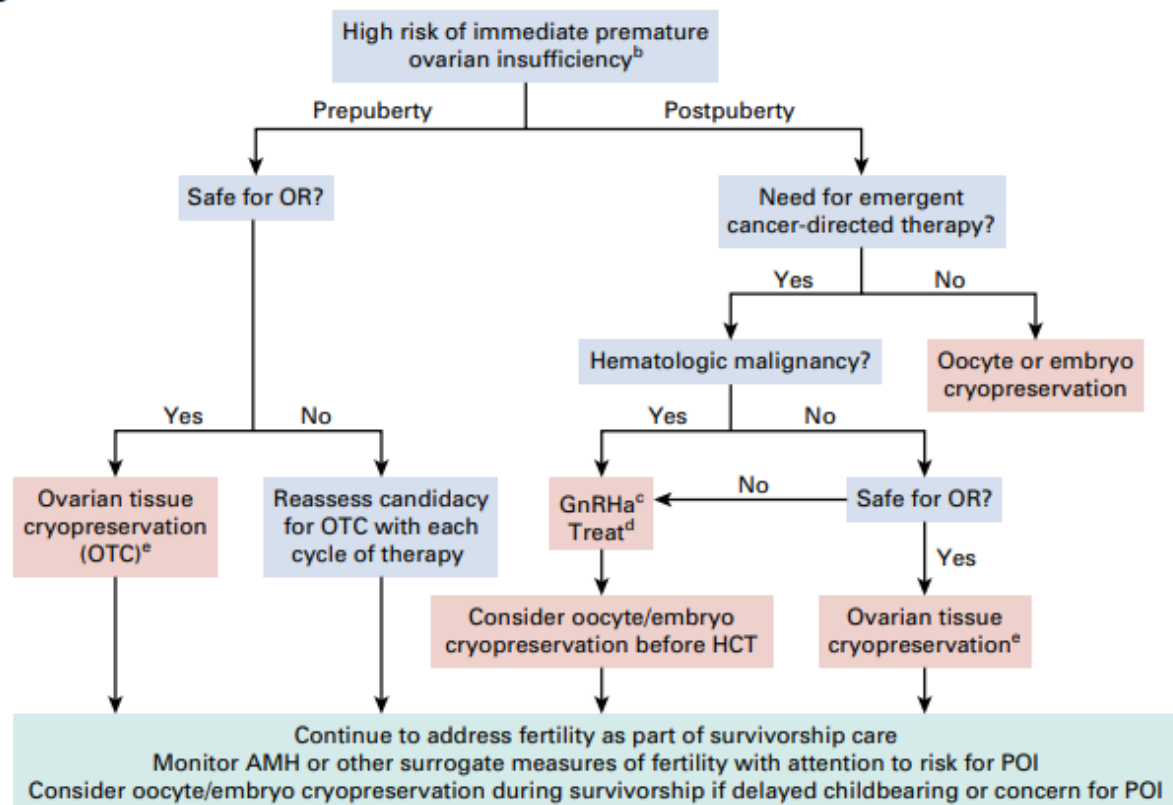


TABLE 2. Female Fertility Preservation Options

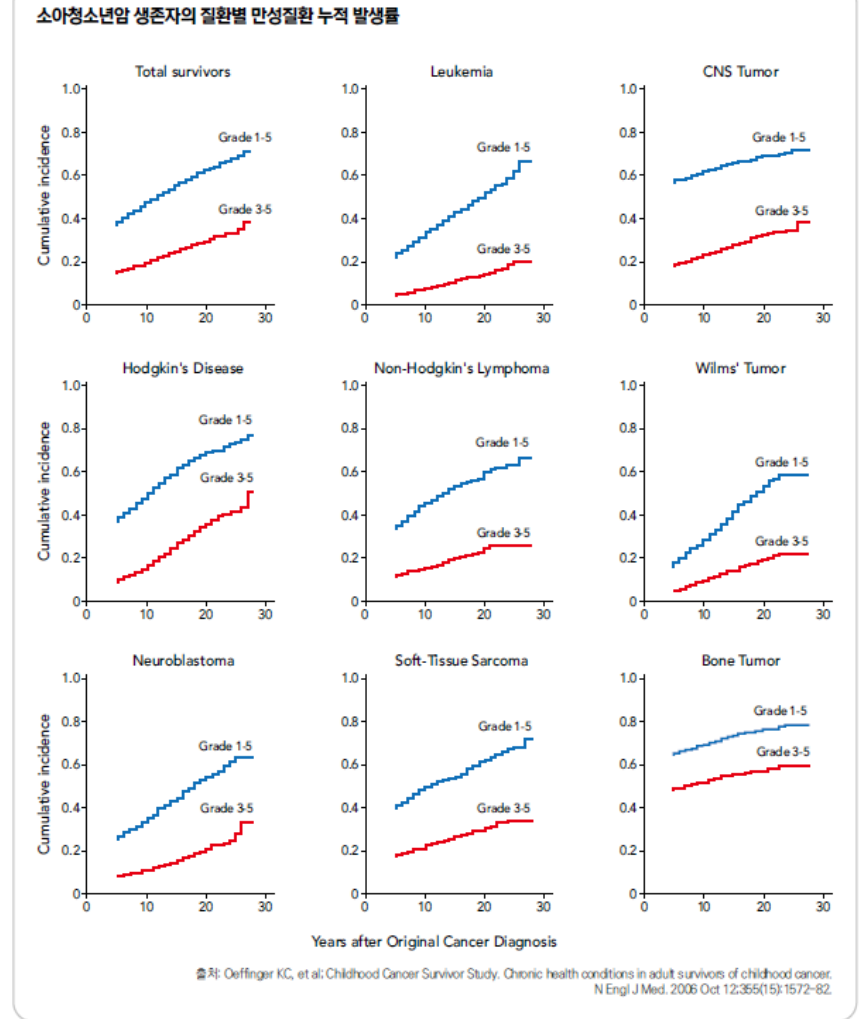
Method	Description	Research	Timing	Comments
Oocyte cryopreservation	Ovarian stimulation followed by oocyte harvest. Oocytes cryopreserved	No	Before or 6-12 months after therapy	Offers advantage to female patients who do not have identified male partner Will need ART to achieve pregnancy
Embryo cryopreservation	Ovarian stimulation followed by oocyte harvest. Combined with sperm to create embryos and cryopreserved	No	Before or 6-12 months after therapy	Gold standard Will need ART to achieve pregnancy
Ovarian tissue cryopreservation	Ovarian tissue surgically removed and cryopreserved	No; however, very limited data with prepubertal cryopreserved ovarian tissue	Before or during therapy	Ovarian tissue transplantation carries risk of malignant cells May achieve pregnancy without ART

Abbreviation: ART, artificial reproductive technology.

Late Effects of Treatment for Childhood Cancer

Among adults who were treated for cancer during childhood, late effects contribute to a high burden of morbidity.

- 60% to more than 90% of survivors develop one or more chronic health conditions.
- 20% to 80% of survivors experience severe or life-threatening complications during adulthood.
- Morbidity accumulation is accelerated in young adult survivors of childhood cancer, compared with that of siblings and the general population. Accumulation of chronic diseases predicts risk of early mortality.



Late Effects of Treatment for Childhood Cancer

The common late effects of pediatric cancer encompass several broad domains, including the following:

- Growth and development; Organ function; Reproductive capacity and health of offspring; Secondary carcinogenesis.
- Psychosocial sequelae related to the primary cancer, its treatment, or maladjustment associated with the cancer experience.

Cancer-related factors	Treatment-related factors	Host-related factors
<ul style="list-style-type: none"> •Organs or tissues affected by the cancer. •Direct tissue effects. •Cancer-induced organ dysfunction or other tissue effects. 	<ul style="list-style-type: none"> •Radiation therapy: Total dose, fraction size, organ or tissue volume exposed. •Chemotherapy: Agent type, dose-intensity, cumulative dose, schedule. •Surgery: Technique, site, consequential organ dysfunction. •HSCT. •Combined-modality effects (therapeutic interactions). •Blood product transfusion. •Chronic graft-versus-host disease. 	<ul style="list-style-type: none"> •Sex. •Genetic predisposition. •Premorbid, comorbid, posttreatment health states and exposures. •Developmental status (age). •Time from diagnosis/therapy. •Inherent tissue sensitivities and capacity for normal tissue repair. •Hormonal milieu. •Socioeconomic status. •Health habits.

Long-Term Follow-Up Guidelines

for Survivors of Childhood, Adolescent, and Young Adult Cancers

Version 6.0 - October 2023

CHILDREN'S
ONCOLOGY
GROUPWebsite: www.survivorshipguidelines.org
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CHEMOTHERAPY

ALKYLATING AGENTS (CONT)

Sec #	Therapeutic Exposure	Potential Late Effects	Periodic Evaluation	Health Counseling/ Further Considerations
14 (female)	Classical Alkylating Agents Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiopeta Heavy Metals Carboplatin Cisplatin Non-Classical Alkylators Dacarbazine (DTIC) Temozolomide	Ovarian hormone deficiencies Delayed puberty Arrested puberty Premature ovarian insufficiency/Premature menopause	HISTORY Onset and tempo of puberty Menstrual history Sexual function (vaginal dryness, libido) Menopausal symptoms Medication use Yearly PHYSICAL Tanner staging until sexually mature Yearly Monitor growth until mature Yearly	HEALTH LINKS Ovarian and Reproductive Health COUNSELING Higher cumulative doses of alkylating agents with or without radiation may increase risk. Dose can be estimated using CED dose calculation. Adverse impact of ovarian hormone deficiencies on growth, bone mineralization, cardiovascular disease and sexual dysfunction. POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION FSH and estradiol and/or endocrine/gynecology referral for patients with: <ul style="list-style-type: none"> • No signs of puberty by age 13 years • Failure of pubertal progression • Abnormal menstrual patterns or menopausal symptoms • Ovarian hormone deficiency/insufficiency to weigh risks and benefits of hormonal replacement therapy Bone density evaluation in patients with ovarian hormone deficiencies.
Commonly used alkylators can be converted to a cyclophosphamide equivalent dose by using: CED (mg/m ²)= 1.0 (cumulative cyclophosphamide dose (mg/m ²)) + 0.244 (cumulative ifosfamide dose (mg/m ²)) + 0.857 (cumulative procarbazine dose (mg/m ²)) + 14.286 (cumulative chlorambucil dose (mg/m ²)) + 15 (cumulative BCNU dose (mg/m ²)) + 16 (cumulative CCNU dose (mg/m ²)) + 40 (cumulative melphalan dose (mg/m ²)) + 50 (cumulative thiopeta dose (mg/m ²)) + 100 (cumulative nitrogen mustard dose (mg/m ²)) + 8.823 (cumulative busulfan dose (mg/m ²))				SYSTEM = Reproductive (Female) SCORE Classical Alkylating Agents = 1 Heavy Metals = 2B Non-Classical Alkylators = 2A

Additional Information

Alkylating agent doses that cause gonadal dysfunction show individual variation. Females can typically maintain gonadal function at higher cumulative doses than males.

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health conditions, and health behaviors that may increase risk.

- Patient factors: Older age at treatment
- Cancer/Treatment factors: Higher cumulative doses of alkylators or combinations of alkylators, combination with radiation to abdomen/pelvis, lumbar or sacral spine (from ovarian scatter), or brain/cranium (neuroendocrine axis), any alkylators combined with pelvic radiation or TBI
- Health behaviors: Smoking

Table 2. Key points of AYA-specific survivorship.

Focus on AYA-Specific Survivorship Issues

Physical, e.g.,

- o Second malignancies
- o Cardiovascular disease
- o Endocrine dysfunction
- o Neurocognitive deficits
- o Fertility
- o Sexual dysfunction
- o Body disfigurement
- o Physical condition

Psychological, e.g.,

- o Psychological distress
- o Posttraumatic stress
- o Fear of recurrence

Social, e.g.,

- o Education, employment, and financial challenges
 - o Relationships
-

AYA Cancer Survivorship Research:

- Access to appropriate trials
 - Pooling different data sources (e.g., PROs, clinical outcomes)
 - Development of standardized core outcome set
-

AYA Cancer Survivorship Care:

- Improving information provision and communication (e.g., SCP)
 - Access to preventative measures (e.g., HPV vaccination)
 - Access to appropriate treatment and expert services
 - Development of AYA cancer survivorship programs (risk-stratified)
 - Development of evidence-based AYA cancer survivorship guidelines
 - Monitoring of provided care (e.g., performance indicators)
-



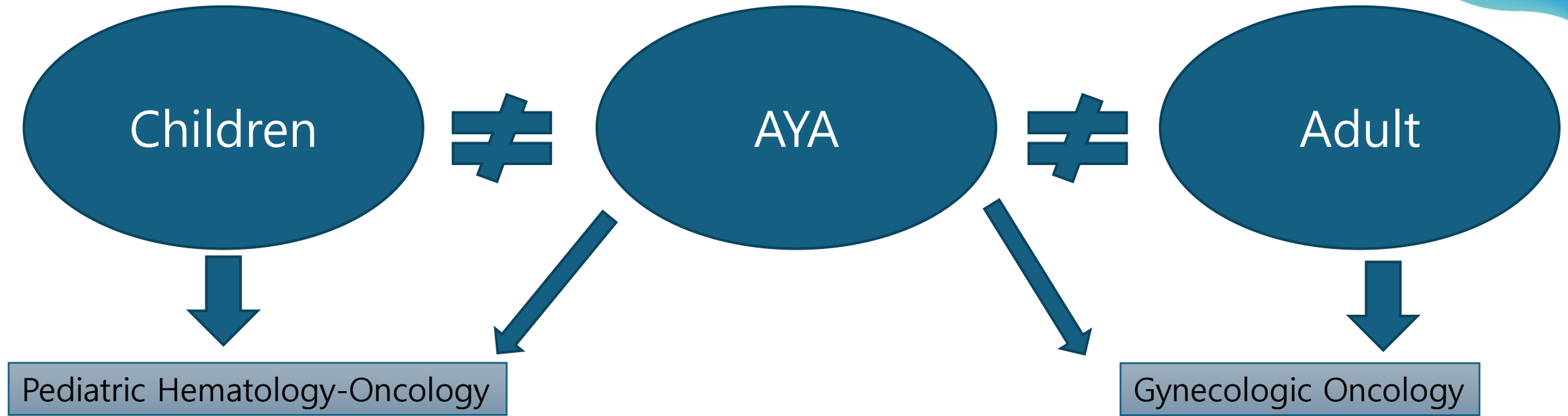
NCCN AYA Survivors Screening Recommendations

Treatment	Risk	Screening
Radiation to HPA axis	Growth hormone deficiency ($\geq 18\text{Gy}$) Central hypothyroidism ($\geq 15\text{Gy}$) Gonadotropin deficiency ($\geq 30\text{Gy}$) Central adrenal insufficiency ($\geq 30\text{Gy}$)	Ht, Wt, BMI q6 Mo TSH, free T4, yearly FSH, LH, AMH 8A serum cortisol, yearly
[High risk] cumulative anthracycline ≥ 250 mg/m² ; chest RT ($\geq 30\text{Gy}$); anthracycline ≥ 100 mg/m ² + chest RT ($\geq 15\text{Gy}$) [Moderate risk] cumulative anthracycline 100-250 mg/m ² ; chest RT alone (15-30Gy)	Cardiomyopathy/asymptomatic heart failure	치료 종료 후 baseline ECG Echocardiogram (q2 year for high risk/ q5 year for moderate risk)
[High risk] chest RT ($\geq 35\text{Gy}$)	Valvular heart disease	Echocardiogram (q2 year)
Chest RT ≥ 15 Gy; TBI (≥ 6 Gy in single fraction or ≥ 12 Gy fractionated); partial tholacic RT (mean lung dose ≥ 146 Gy); bleomycin ; bleomycin + chest RT ; busulfan, carmustine	폐기능 저하, 폐섬유화	PFT (post-therapy baseline, and then clinically indicated)
Radiation include thyroid gland, use of ICI	Hypothyroidism, thyroid cancer, hyperthyroidism	TSH, free T4, thyroid/neck exam, yearly

Treatment	Risk	Screening
<p>[High level of risk]</p> <ul style="list-style-type: none"> – Alkylator: Prepubertal (>12 g/m² CED); pubertal (>8 g/m² CED) – HCT: Including alkylator + TBI; myeloablative and reduced-intensity regimens – Radiation to ovary: Prepubertal (≥15 Gy); pubertal (≥10 Gy) – Radiation to hypothalamus: >40 Gy <p>[Significantly increased risk]</p> <ul style="list-style-type: none"> – Alkylator: Prepubertal (8–12 g/m² CED); pubertal (4–8 g/m² CED) – Radiation to ovary: Prepubertal (<15 Gy); pubertal (<10 Gy) – Radiation to hypothalamus: 30–39 Gy <p>[Minimally increased risk]</p> <ul style="list-style-type: none"> – Alkylator: Prepubertal (<8 g/m² CED); pubertal (<4 g/m² CED) – Carboplatin or cisplatin: Any dose – Radiation to hypothalamus: 22–29.9 Gy 	<p>Acute ovarian insufficiency or primary ovarian insufficiency</p>	<p>Annual history and physical (H&P) (menstrual and pregnancy history, history of hormonal therapy, Tanner staging) only.</p> <p>Laboratory screening (ie, FSH, estradiol, AMH) for those with menstrual cycle dysfunction or those who desire information about future fertility.</p> <p>Bone density evaluation (dual-energy x-ray absorptiometry [DEXA]) at baseline (entry into long-term follow-up) for those who had corticosteroids and/or HCT only.</p>
<p>Cisplatin ≥ 360 mg/m², carboplatin conditioning for HCT, RT involving ear (≥30 Gy), combination cisplatin + RT</p>	<p>Ototoxicity</p>	<p>Audiology testing (post-therapy baseline and then every 5 years)</p>
<p>Radiation ≥10 Gy, combination of radiation with nephrotoxic agents (eg, cisplatin, ifosfamide, aminoglycosides, amphotericin, immunosuppressants), history of HCT, and history of nephrectomy</p>	<p>Kidney insufficiency and secondary kidney/renovascular hypertension</p>	<p>Post-therapy baseline blood urea nitrogen (BUN), creatinine, Na, K, Cl, CO₂, Ca, Mg, and PO₄; repeat as clinically indicated; measure blood pressure yearly</p>
<p>Cyclophosphamide >3 g/m², ifosfamide, and pelvic radiation ≥30 Gy</p>	<p>Hemorrhagic cystitis/bladder fibrosis</p>	<p>Screening of pertinent urinary tract symptoms is recommended.</p>
<p>Cyclophosphamide combined with pelvic radiation</p>	<p>Bladder cancer</p>	<p>Screening of pertinent urinary tract symptoms is recommended.</p>

NCCN AYA Survivors Screening Recommendations

Treatment	Risk	Screening
방사선 치료 전반	Secondary malignancy	치료 부위 인접 장기 중심 선별
Thoracic RT	Breast cancer	30세미만 생존자에서 조기 선별 검사
Abdominal/pelvic RT, TBI, spinal RT	Colorectal cancer	colonoscopy every 5 years, multitarget stool DNA/RNA-based test every 3 years, or blood-based cell-free DNA test every 3 years ; starting at age 30 or 5 years after radiation, whichever occurs last.
Epipodophyllotoxins, alkylating agents, heavy metals, and/or anthracyclines ; autologous HCT	t-AML or Myelodysplasia	CBC and bone marrow exam as clinically indicated based on symptoms; 치료 약제 노출 후 10년이 경과하면 위험도는 현저히 감소
모든 AYA 생존자	우울, 불안, PTSD	• 정기적 정신건강 선별
모든 AYA 생존자	흡연·음주·약물 사용	• 위험행동 선별 및 중재
모든 AYA 생존자	후기 부작용 (late effects)	• Survivorship Care Plan 수립• 평생 추적관리
치료 종료 후	진료 단절	• Primary Care Provider(PCP) 연계 및 transition of care



- Unique biological, reproductive, and psychosocial needs
- Chemotherapy-related gonadotoxicity -> Ovarian insufficiency & infertility -> Early, individualized fertility counseling and preservation strategies (Referral to reproductive endocrinology)
- Late effects in long-term survivors -> Multidisciplinary care models

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Thank you for your attention!



대한부인종양학회
Korean Society of Gynecologic Oncology

