FONDAZIONE ITALIANA LINFOMI

LATE EFFECTS
GUARIRE DAL LINFOMA E VIVERE BENE

Seconde neoplasie: prevenzione e diagnostica

Bari, 17-18 febbraio 2023

Sala “A. Leogrande”
Centro Polifunzionale Studenti
Università degli Studi di Bari “Aldo Moro”

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Disclosures of Luca Nassi

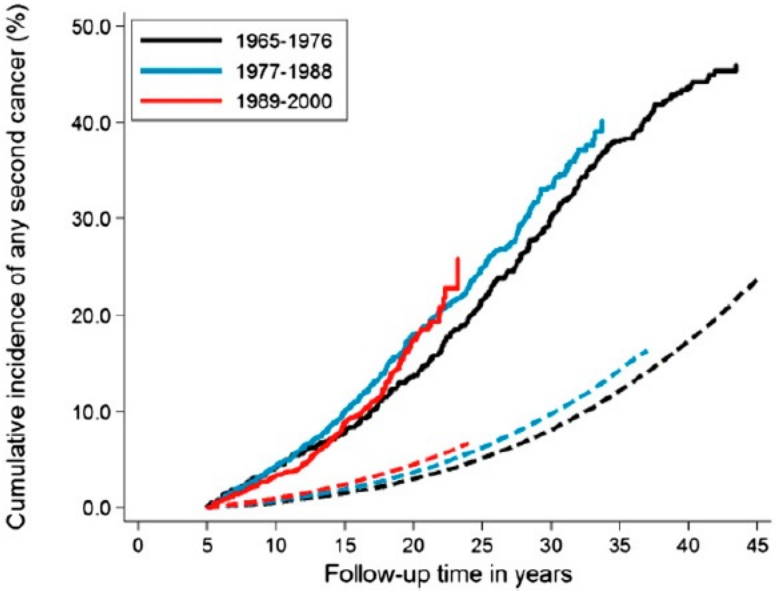
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Takeda					X	X	
Roche						X	
Janssen	X				X		
Kyowa Kirin					X	X	
Incyte						X	
EUSApharma					X		

Second malignancies: a well recognized risk

- Increasead risk of SM (both solid and hematological) in lymphoma survivors
- Role of chemotherapy and radiotherapy
- Period of treatment (type of drugs, doses and fields of radiotherapy)
- Age at treatment, hormonal status
- Lifestyles

Bonadonna G et al; N Engl J Med 1973; 288:1242
van Leeuwen FE et al. Hematology 2016; 2016:323
Travis LB et al. J Natl Cancer Inst 2006; 98:15
Bessell EM et al; Br J Cancer 2012; 107:531

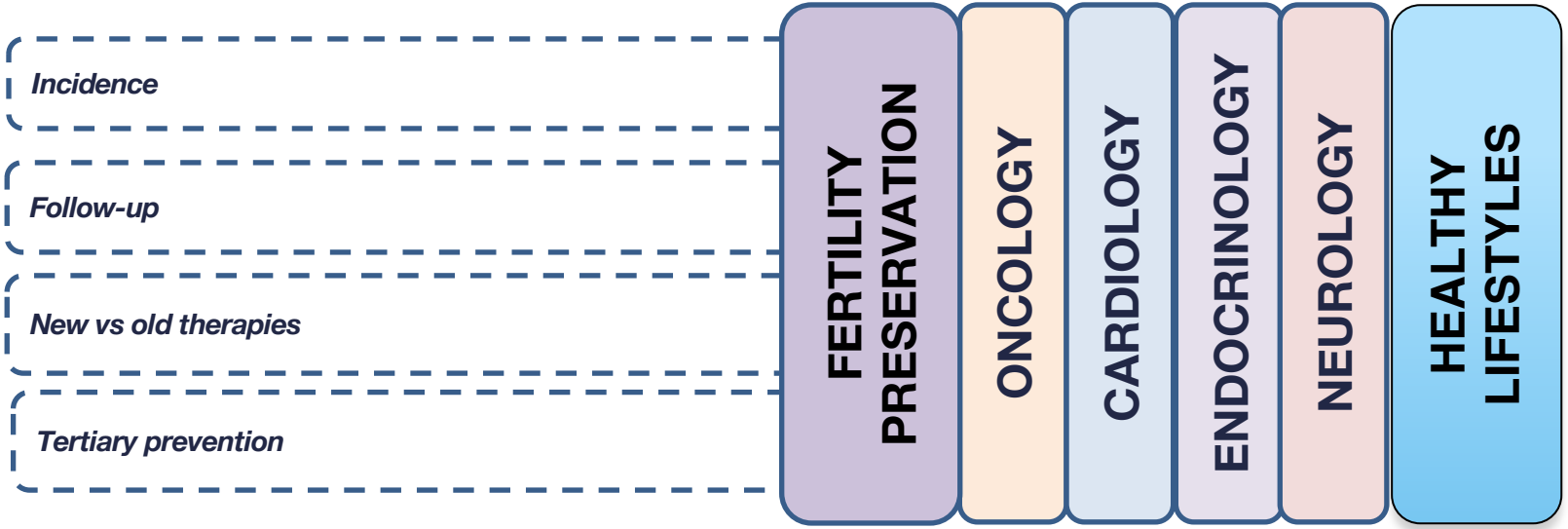
Second malignancies: a well recognized risk



Cumulative incidence 40 years after HL: **43.6%**

van Leeuwen FE et al. Hematology 2016; 2016:323

Fondazione Italiana Linfomi systematic review



Gerardi C et al. Cancers MDPI 2021; 2013:2976

Fondazione Italiana Linfomi systematic review
Second malignancies PICOs

PICO A: What is the incidence of SM in cHL or DLBCL long-term survivors after first or second line treatments?

PICO B: Has the incidence of SM in cHL or DLBCL long-term survivors who underwent first or second line chemotherapy and ASCT changed with the introduction of modern radiotherapy?

PICO C: Are planned follow-up/screening schemes effective for the management and early diagnosis of second cancers in cHL or DLBCL long-term survivors treated, regardless of the type of CHT/RT (first and second line including ASCT)?

cancers

Systematic Review

Second Cancers in Classical Hodgkin Lymphoma and Diffuse Large B-Cell Lymphoma: A Systematic Review by the Fondazione Italiana Linfomi

Luca Nassi [1,*], Vitaliana De Sanctis [2], Giacomo Loseto [3], Chiara Gerardi [4], Eleonora Allocati [4], Sabino Ciavarella [3], Carla Minoia [3], Attilio Guarini [3] and Alessia Bari [5]

Special Issue "Lymphoma Survivorship"

Guest Editors
Francesco Merli
Monica Balzarotti
Alessandra Tucci

PI
Attilio Guarini

Academic Editor
Elaine Jaffe

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Research strategies

('hodgkin disease'/exp OR 'hodgkin disease' OR 'diffuse large b cell lymphoma')
AND
('consolidation chemotherapy' OR 'induction chemotherapy' OR 'conventional chemotherapy' OR 'chemotherapy' OR 'chemotherapy'/exp OR 'cyclophosphamide plus doxorubicin plus prednisolone plus rituximab plus vincristine' OR 'cyclophosphamide doxorubicin vincristine prednisone' OR 'chop protocol' OR 'abvd protocol' OR 'high dose protocol' OR 'high dose chemotherapy' OR 'autologous stem cell transplantation' OR 'transplantation' OR 'hematopoietic stem cell graft' OR 'hematopoietic stem cell transplantation' OR 'brentuximab' OR 'antineoplastic agent' OR 'antineoplastic agent'/exp OR 'antineoplastic protocol' OR 'adjuvant chemotherapy' OR 'chemoradiotherapy' OR 'adjuvant chemoradiotherapy')
AND
('long term survival' OR 'long term survival'/exp)
AND
('second cancer' OR 'second cancer'/exp OR 'second tumor' OR 'neoplasm radiotherapy' OR 'radiation induced neoplasm' OR 'radiation induced neoplasm'/exp OR 'lymphoma relapse' OR 'lymphoma recurrence')

ID	Search
#1	Hodgkin's disease
#2	MeSH descriptor: [Hodgkin Disease] explode all trees
#3	Hodgkin's lymphoma
#4	B-cell lymphoma
#5	MeSH descriptor: [Lymphoma, B-Cell] explode all trees
#6	#1 OR #2 OR #3 OR #4 OR #5
#7	"consolidation chemotherapy" OR "induction chemotherapy" OR "conventional chemotherapy" OR "chemotherapy" OR "cyclophosphamide plus doxorubicin plus prednisolone plus rituximab plus vincristine" OR "cyclophosphamide doxorubicin vincristine prednisone" OR "chop protocol" OR "abvd protocol" OR "high dose protocol" OR "high dose chemotherapy" OR "autologous stem cell transplantation" OR "transplantation" OR "hematopoietic stem cell graft" OR "hematopoietic stem cell transplantation' OR 'brentuximab" OR "antineoplastic agent" OR "antineoplastic protocol" OR "adjuvant chemotherapy" OR "chemoradiotherapy" OR "adjuvant chemoradiotherapy"
#8	MeSH descriptor: [Drug Therapy] explode all trees
#9	MeSH descriptor: [Antineoplastic Agents] this term only
#10	#7 OR #8 OR #9
#11	'long term surv*'
#12	MeSH descriptor: [Cancer Survivors] explode all trees
#13	#11 OR #12
#14	"second cancer" OR "second tumor" OR "neoplasm radiotherapy" OR "radiation induced neoplasm" OR "lymphoma relapse" OR "lymphoma recurrence"
#15	MeSH descriptor: [Neoplasms, Second Primary] explode all trees
#16	MeSH descriptor: [Neoplasms, Radiation-Induced] explode all trees
#17	#14 OR #15 OR #16
#18	#6 AND #10 AND #13 AND #17
#19	"accession number" near pubmed
#20	"accession number" near EMBASE
#21	#19 OR #20
#22	#18 NOT #21

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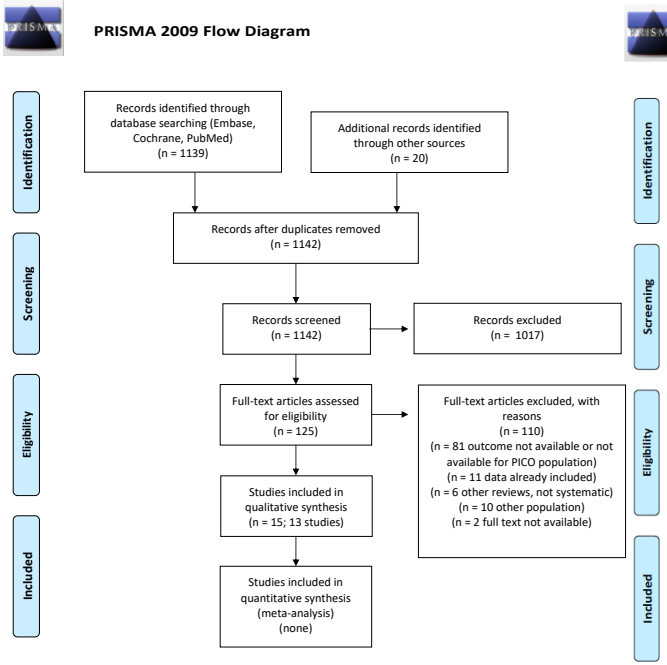

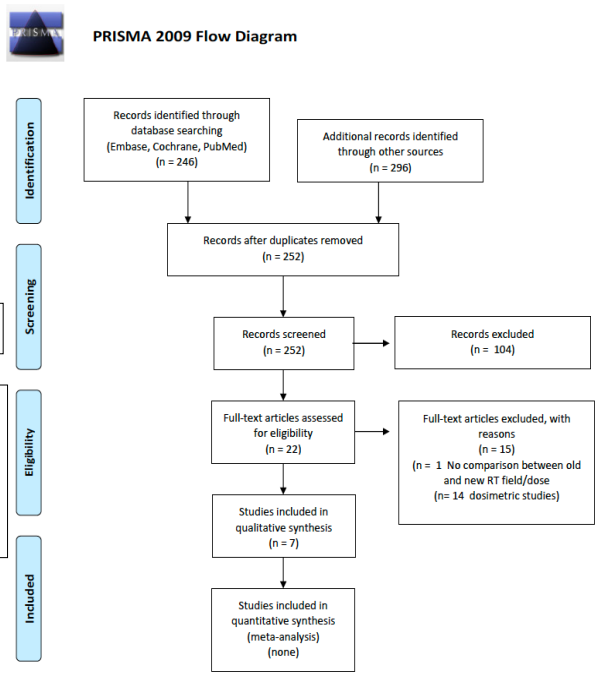

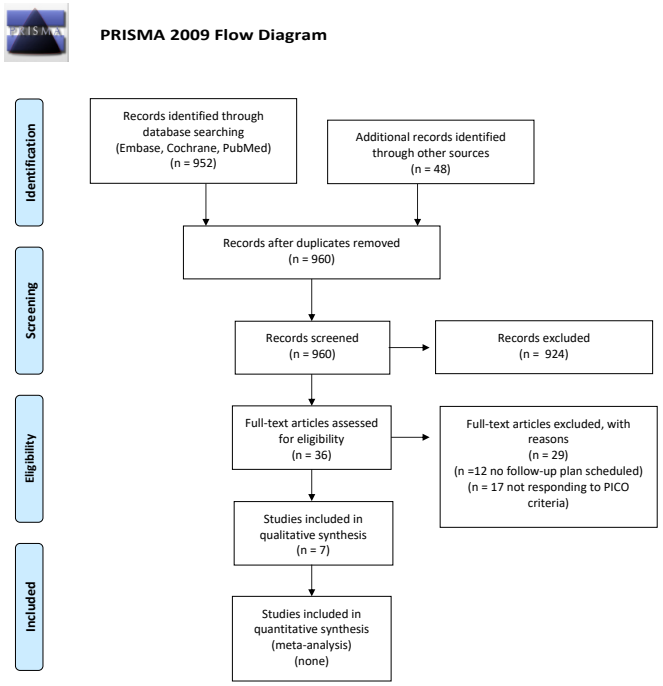

2354 abstracts reviewed; 29 papers selected

FIL systematic review on SM: PICO A

- Higher risk of malignancies in cHL patients treated with ABVD vs general population; risk increased over time also after 10-15 years from therapy;
- cHL first-line treatment with BEACOPP is associated with a higher risk of SM than ABVD (9.6 per 1000 PY vs 6.3 per 1000 PY, 7y median FU);
- DLBCL first-line treatment with R-CHOP is associated to a moderate increased risk of SM (10.8% at 10y FU);
- Second-line treatments with ASCT are associated to higher rates of SM (12-15% at 15y FU), with a higher incidence of myeloid SM.

Cancers MDPI 2022; 14:519

FIL systematic review on SM: PICO B

- Lower incidence of SM in cHL patients treated with smaller volumes and lower doses (IFRT vs EFRT), particularly for breast cancer and lung cancer;

- Smaller RT field sizes (involved nodal and involved site RT) may lead to a further reduction of the incidence of SM.

Cancers MDPI 2022; 14:519

FIL systematic review on SM: PICO C

- Selected papers according to PICO methodology only for breast cancer screening in cHL patients treated with RT;
- Low consciousness in survivors of the increased risk of SM;
- Combining US/Mx and MRI could increase the diagnostic sensitivity;
- Immediate planned surveillance program at the beginning of FU could obtain a greater compliance.

Cancers MDPI 2022; 14:519

FIL systematic review on SM: recommendations

Monitoring strategies should be individualized, depending on RT dose, type of CT regimen, age at therapy, and predisposing factors (family history, sex, behavioral risk factors).

No evidence of screening programs for DLBCL survivors.

Breast cancer: for patients treated with >10 Gy RT on the chest: start at age 40 or 8 years after RT, whichever comes first, by annual Mx, add annual breast MRI for women who received chest RT between ages 10–30 years.

Lung cancer: annual chest LDCT scan for smokers treated with alkylators/RT.

Skin cancer: annual skin evaluation of the irradiated skin areas.

Thyroid cancer: neck ultra-sound for pts treated with neck RT.

Colorectal cancer: annual FOB and colonoscopy every 10 years (based on findings) for pts treated with abdominal RT (≥20 Gy), starting from the age of 30 years or 5 years after RT.

MDS/AML: annual blood cell count evaluation.

NCCN recommendations

Subsequent new primary malignant neoplasms may occur in survivors years after treatment when the survivor's oncologist may no longer be involved in the survivor's care.

The overall cancer rate in survivors is higher than in the general population. This increased risk is due to genetic susceptibilities (eg, hereditary cancer syndromes) and/or family history, shared etiologic exposures (eg, smoking, environmental exposures, health behaviors, HPV), and mutagenic effects of cancer treatment. Health behaviors should be modified as possible (eg, smoking cessation, weight management) to decrease the risk of subsequent malignancies.

Treatment-related subsequent primary cancers vary with the type and intensity of anticancer treatment and are associated in particular with radiation and specific chemotherapeutic agents.

Evidence suggests that excess lifetime radiation exposure from CT imaging may be associated with a mildly increased risk of developing a radiation-associated cancer. Use of radiologic studies to screen for recurrent cancer should be based on diagnosis and evidence that early detection of recurrence will improve cancer-related outcomes.

NCCN v1.2022, 30/03/2022

NCCN recommendations

Thyroid cancer: annual neck exam, neck ultrasound as clinically indicated.

Skin cancer: consider annual skin exam and/or dermatology referral, counsel on sun safety and regular use of sunscreen (at least SPF 30).

Breast cancer: breast MRI and Mx annually, starting at age 30 or 8 years after radiation, whichever occurs last, for exposure ≥10 Gy and <30 years old.

Lung cancer: consider imaging if clinically indicated due to signs or symptoms of disease. Smoking substantially increases risk. For smokers and former smokers: counsel on tobacco cessation as indicated, consider spiral CT scan or referral to lung cancer screening clinic for shared decision-making if screening criteria met, for survivors not meeting lung cancer screening criteria (especially survivors of cHL), consider chest imaging as clinically indicated.

Colorectal cancer: screening starting at age 30 or 5 years after radiation, whichever occurs last, for exposure ≥20 Gy. Repeat colorectal cancer screening based on findings, in consultation with primary care, gastroenterologist, or oncologist.

AML/MDS: CBC if clinically indicated due to signs or symptoms of disease.

NCCN v1.2022, 30/03/2022

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