GdL AIEOP
Effetti tardivi delle terapie antiblastiche

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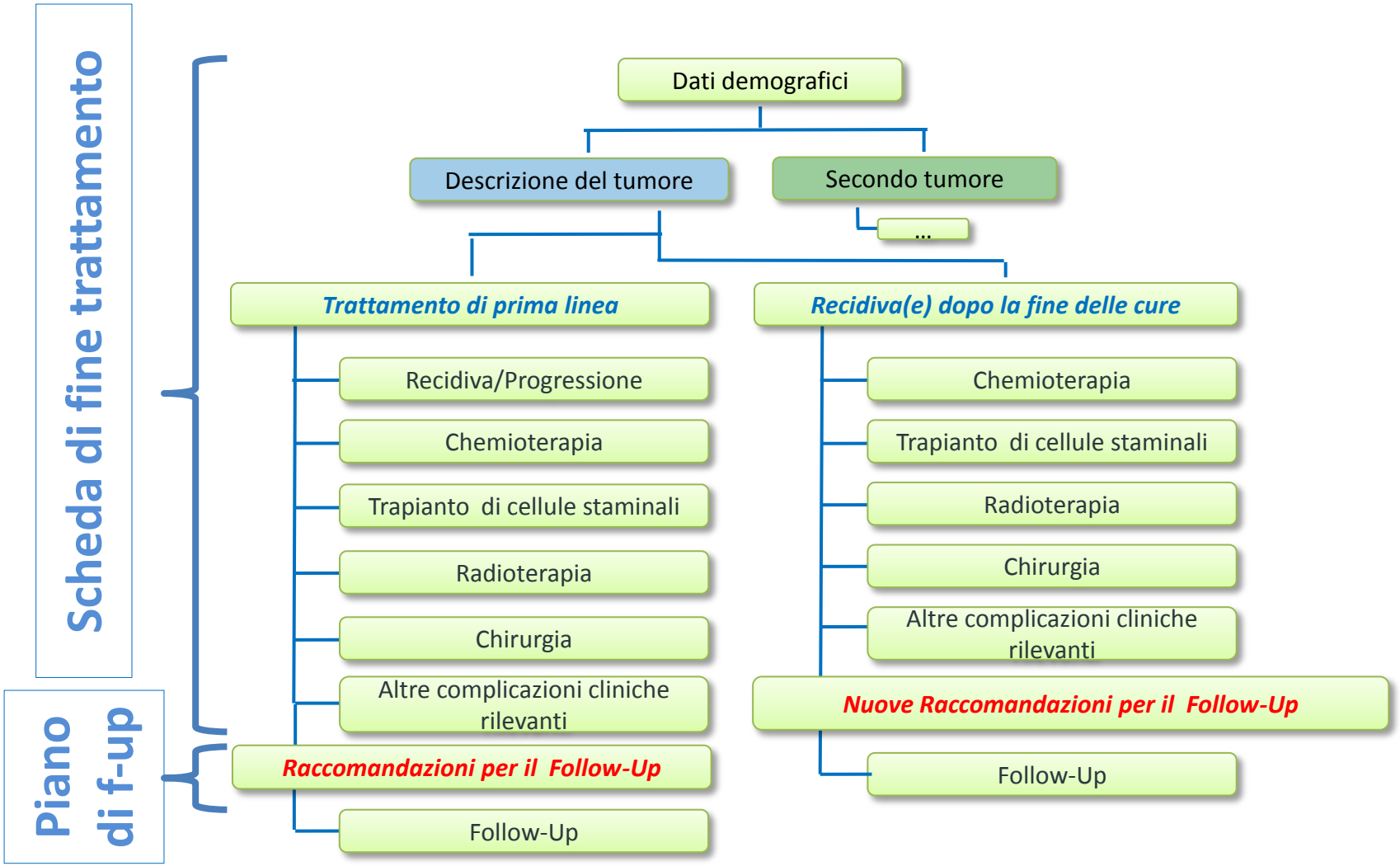
Ordine del giorno

- **Passaporto del lungo-sopravvivente (SurPass)**
  - Aggiornamento su fase test implementazione Passaporto del lungo-sopravvivente – criticità e proposte di modifica
  - Proposta di sostituzione linee guida pragmatiche AIEOP con quelle PanCare (PanCareFollowUP) e conseguente aggiornamento lista variabili SurPass)
  - Scheda di follow-up del Passaporto
  - Estensione del SurPass a tutti i centri AIEOP
- **ROT**
  - Migrazione del ROT su piattaforma AIEOP
  - Protocollo ROT: nuovo emendamento o nuovo protocollo
- **Progetto COVID di PanCare**
  - questionario
  - partecipazione riunioni

Struttura del Passaporto del lungo-sopravvivente



Implementazione in 7 centri AIEOP







Fondazione Pino Camerani ed Elisabetta Pintaldi

Care plan based on IGHG /PanCare Guidelines

✓ 6 IGHG published

- Secondary breast cancer
- Cardiomyopathy
- Premature ovarian insufficiency
- Male gonadotoxicity
- Thyroid Cancer
- Ototoxicity

✓ 10 IGHG completed but not published yet

- Secondary CNS tumors
- Secondary GI neoplasms
- Cardiovascular toxicity
- Metabolic syndrome
- Hypotalamic-Pituitary dysf.
- Bone health
- Pulmonary dysfunction
- Renal toxicity
- Throid dysfunction
- Mental health

✓ 16 PCFU consensus-based recommendations (pragmatic)

- Spleen and immunological abnorm.
- Craniofacial growth disturbances
- Chronic sinusitis
- Dental abnormalities
- Gastrointestinal abnormalities
- Lower urine tract abnorm.
- Melanoma non m. skin cancer
- Alopecia
- Spine scoliosis and kyphosis
- Visual abnormalities
- Behaviour disorders
- Epilepsy
- Arrhytmia
- Valvular heart disease
- Pericardial disease
- Other SMN

Approccio pragmatico AIEOP per raccomandazioni ancora mancanti da IGHG/PanCare

Organo a rischio	Possible complicazione
Cuore	Valvulopatie, Arritmie, Ischemia
Tiroide	Distiroidismo
Gastro Intestinale	Secondi tumori
Asse Ipotlamico/Ipofisario	Ritardo di crescita, Deficit di altre tropine
Rene	Tubulopatia e glomerulopatia
Vescica	Fibrosi, Tumore secondario
Udito	Sordità
Occhio	Cataratta, Secchezza oculare
Cute	Secondo tumore
Fegato	Fibrosi/Cirrosi, Epatite
Sindrome metabolica	
SNC	Secondo tumore, Deficit cognitivo, Leucoencefalopatia
Denti	Ipo/agenesia, Difetti dello smalto

Statistiche descrittive sul SurPass in 6 centri AIEOP

Pazienti	N (%)
Registrati nel sito	1580
Con almeno 1 SurPass emesso	693
LLA	243 (35)
L di Hodgkin	92(13)
Nefroblastoma	58 (8)
Neuroblastoma	51 (7)
T. SNC (Medullo + Astro)	37 (5)
RMS	24 (3)
S di Ewing	27 (4)
Osteosarcoma	10 (1)
Germinoma maligno gonadico	17 (2)
…	… (23)
Passaporti emessi	789
Con almeno 1 raccomandazione **emessa dal sistema**	544
Con almeno 1 raccomandazione **aggiunta dal medico**	314

Raccomandazioni rilasciate in base a tipo di linea guida

Pragmatiche AIEOP	N	%
Vescica	384	21
SNC	264	14
Rene	199	11
Cute	198	11
Ossa	169	9
Sindrome Metabolica	157	8
Fegato	117	6
Udito	77	4
Polmone	77	4
Asse Ipotalamo-Ipofisario	72	4
Vista	63	3
Denti	45	2
Intestino	37	2
Totale	**1859**	**100**

IGHG	N	%
Cardiomiopatia	519	40
Tumore tiroideo	144	11
Tumore al seno	73	6
Insufficenza ovarica	277	21
Spermatogenesi	196	15
Disfunzione sessuale	78	6
Deficit testosterone	22	2
TOTALE	**1309**	**100**

Gran Totale: 3168

Raccomandazioni rilasciate

Raccomandazione	N	%
Cardiomiopatia	519	16,4
Vescica	384	12,1
Insufficenza ovarica	277	8,7
SNC	264	8,3
Rene	199	6,3
Cute	198	6,3
Spermatogenesi	196	6,2
Ossa	169	5,3
Sindrome Metabolica	157	5,0
Tumore tiroideo (SNM)	144	4,5
Fegato	117	3,7
Disfunzione sessuale	78	2,5
Udito	77	2,4
Polmone	77	2,4
Tumore al seno (SNM)	73	2,3
Asse Ipotalamo-Ipofisario	72	2,3
Vista	63	2,0
Denti	45	1,4
Intestino	37	1,2
Deficit testosterone	22	0,7
Totale	**3168**	**100,0**

Raccomandazioni pragmatiche PanCareFollowUP

Awareness only:

- Consensus-based: 1) higher risk groups; 2) surveillance of alopecia; 3) cerebrovascular problems; 4) dental and oral problems; 5) gastro-intestinal problems; 6) peripheral neuropathy.

Awareness, history and/or physical exam without surveillance test

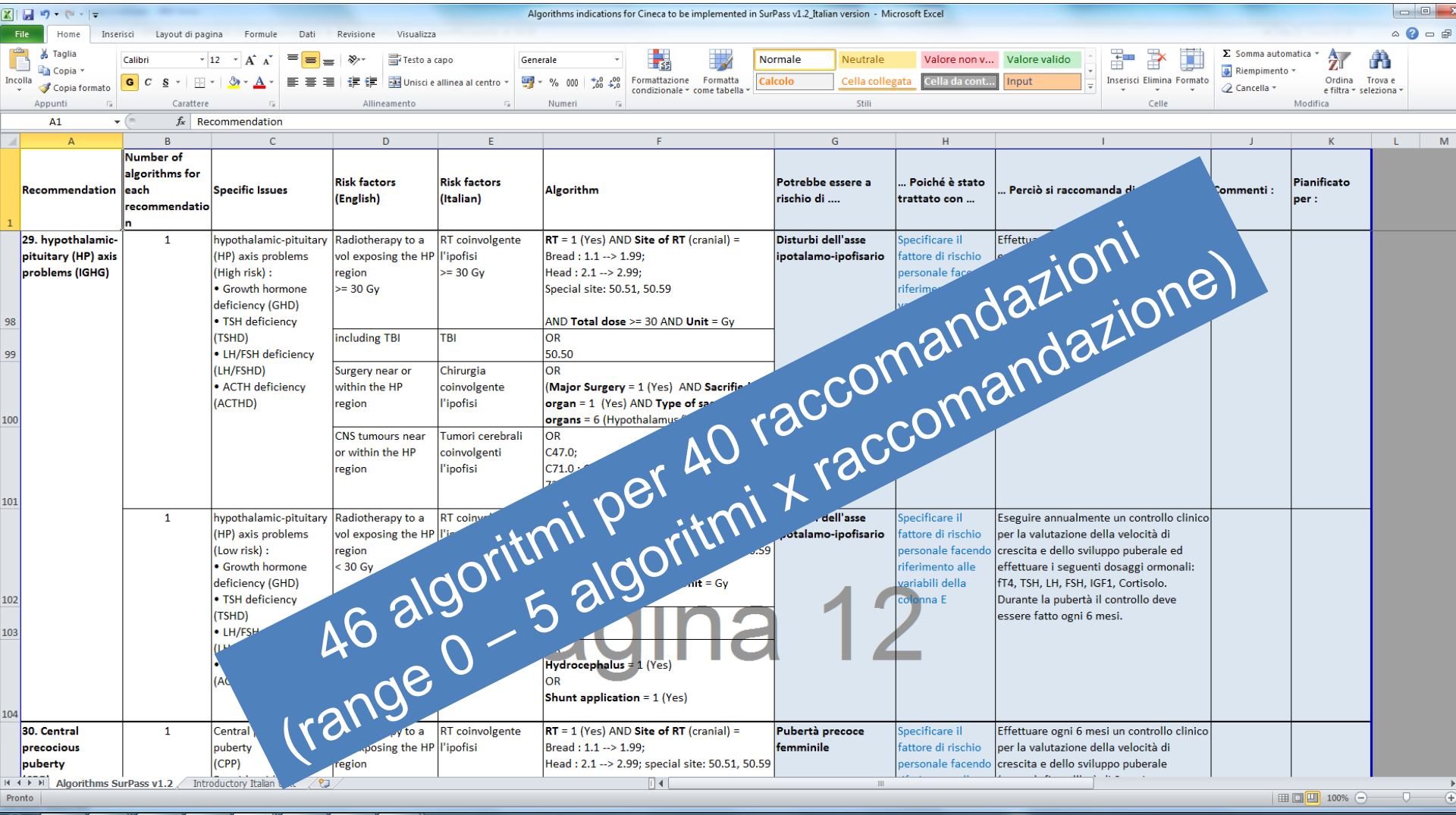
- Evidence-based: 7) cancer-related fatigue (IGHG); 8) obstetric problems (IGHG)
- Consensus-based: 9) health promotion; 10) surveillance of subsequent neoplasms (10.1) Acute myeloid leukaemia or myelodysplasia, 10.2) Bladder cancer, 10.3) Bone cancer, 10.4) Lung cancer, 10.5) Oral cancer; 11) subsequent melanoma and non-melanoma skin cancer; 12) psychosocial problems; 13) mental health problems; 14) chronic pain; 15) neurocognitive problems; 16) eye problems; 17) craniofacial growth problems; 18) spine scoliosis and kyphosis; 19) lower urinary tract problems;

Awareness, history and/or physical exam with potential surveillance test

- Evidence-based: 20) subsequent thyroid cancer (IGHG); 21) subsequent CNS neoplasms (IGHG);

Awareness, history and/or physical exam with surveillance test

- Evidence-based: 22) subsequent breast cancer (IGHG); 23) hypothalamic-pituitary (HP) axis problems (IGHG); 24) central precocious puberty (CPP) (IGHG); 25) ear problems (IGHG); 26) asymptomatic coronary artery disease (IGHG); 27) male fertility problems and sexual dysfunction (IGHG); 28) premature ovarian insufficiency (IGHG)



Algorithms indications for Cineca to be implemented in SurPass v1.2_Italian version - Microsoft Excel

A1: Recommendation

	Recommendation	Number of algorithms for each recommendation	Specific Issues	Risk factors (English)	Risk factors (Italian)	Algorithm	Potrebbe essere a rischio di	... Poiché è stato trattato con ...	... Perciò si raccomanda di	Commenti :	Pianificato per :
98	**29. hypothalamic-pituitary (HP) axis problems (IGHG)**	1	hypothalamic-pituitary (HP) axis problems (High risk) : • Growth hormone deficiency (GHD) • TSH deficiency (TSHD) • LH/FSH deficiency (LH/FSHD) • ACTH deficiency (ACTHD)	Radiotherapy to a vol exposing the HP region >= 30 Gy	RT coinvolgente l'ipofisi >= 30 Gy	**RT** = 1 (Yes) AND **Site of RT** (cranial) = Bread : 1.1 --> 1.99; Head : 2.1 --> 2.99; Special site: 50.51, 50.59 AND **Total dose** >= 30 AND **Unit** = Gy	**Disturbi dell'asse ipotalamo-ipofisario**	Specificare il fattore di rischio personale fac... riferime...	Effettua...		
99				including TBI	TBI	OR 50.50					
100				Surgery near or within the HP region	Chirurgia coinvolgente l'ipofisi	OR (**Major Surgery** = 1 (Yes) AND **Sacrifi...** **organ** = 1 (Yes) AND **Type of sa...** **organs** = 6 (Hypothalamus...					
101				CNS tumours near or within the HP region	Tumori cerebrali coinvolgenti l'ipofisi	OR C47.0; C71.0 ...					
102		1	hypothalamic-pituitary (HP) axis problems (Low risk) : • Growth hormone deficiency (GHD) • TSH deficiency (TSHD) • LH/FSH ...	Radiotherapy to a vol exposing the HP region < 30 Gy	RT coinv...	...59 ...nit = Gy	...dell'asse ...otalamo-ipofisario	Specificare il fattore di rischio personale facendo riferimento alle variabili della colonna E	Eseguire annualmente un controllo clinico per la valutazione della velocità di crescita e dello sviluppo puberale ed effettuare i seguenti dosaggi ormonali: fT4, TSH, LH, FSH, IGF1, Cortisolo. Durante la pubertà il controllo deve essere fatto ogni 6 mesi.		
103											
104						**Hydrocephalus** = 1 (Yes) OR **Shunt application** = 1 (Yes)					
	30. Central precocious puberty	1	Central ... puberty (CPP)	...y to a ...posing the HP region	RT coinvolgente l'ipofisi	**RT** = 1 (Yes) AND **Site of RT** (cranial) = Bread : 1.1 --> 1.99; Head : 2.1 --> 2.99; special site: 50.51, 50.59	**Pubertà precoce femminile**	Specificare il fattore di rischio personale facendo ...	Effettuare ogni 6 mesi un controllo clinico per la valutazione della velocità di crescita e dello sviluppo puberale ...		

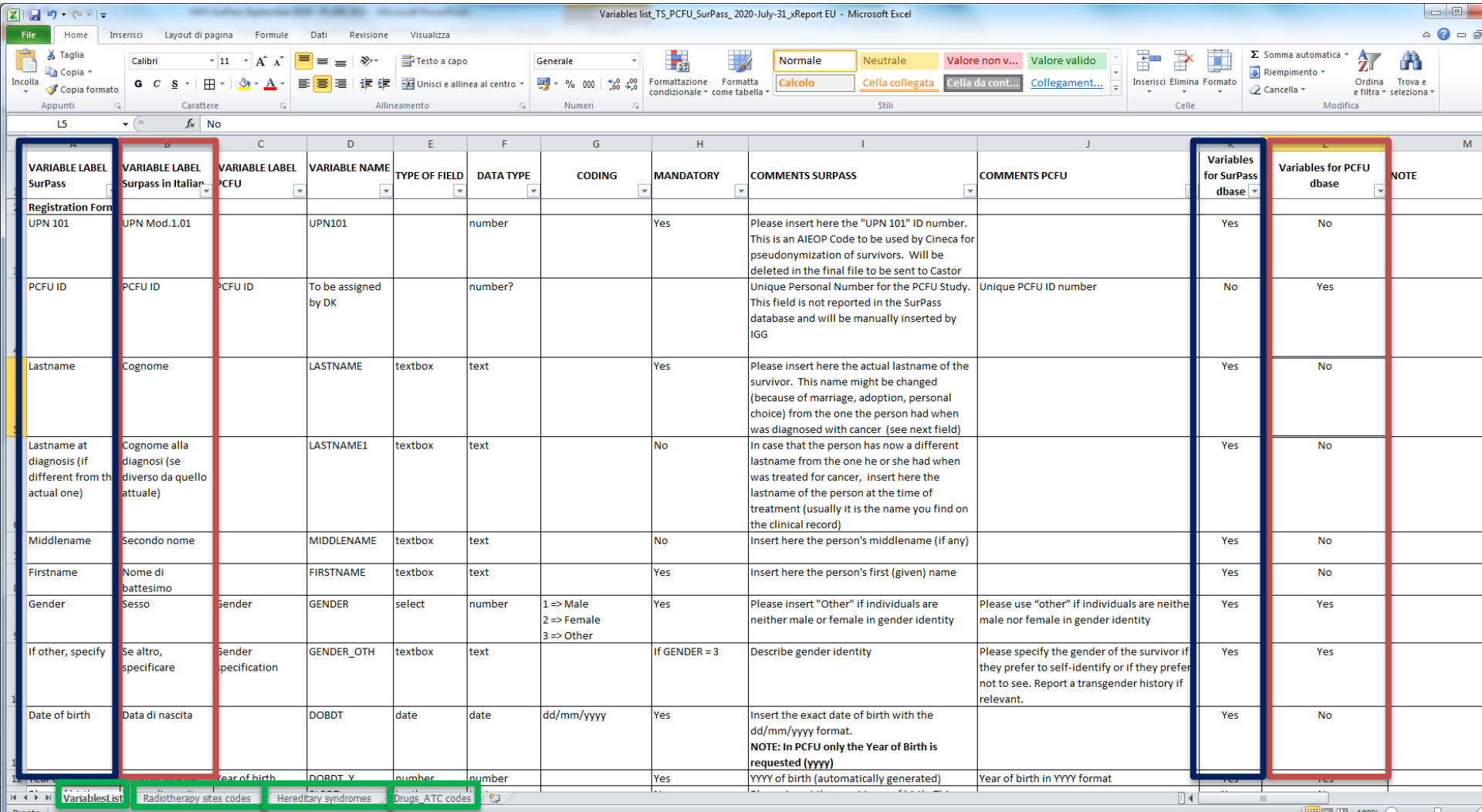
Algorithms SurPass v1.2 | Introductory Italian ...

Pronto

Algoritmi e testo da inserire nelle raccomandazioni personalizzate

Recommendation	Number of algorithms for each recommendation	Specific Issues	Risk factors (English)	Risk factors (Italian)	Algorithm
15. Eye problems	1	Cataract	RT to a vol exposing the lens	RT coivolgente l'occhio	**RT** = 1 (Yes) AND **Site of RT** = 1.1 (Whole brain), 1.98, 1.99 2.1 Orbit/eye, 2.98, 2.99 50.51, 50.59
			Including TBI	TBI	OR 50.50
			Prolonged (at least 4 weeks, continuously) corticosteroids as anti-cancer treatment	Steroidi impiegati nel trattamento antitumorali per almeno 4 settimane continuativamente	OR **CT** = 1 (Yes) AND **Prolonged corticosteroids as anti-cancer treatment at least 4 weeks continuously ?** = Yes
	1	Other eye problems • lacrimal duct atrophy (risk with radioiodine therapy) • xerophtalmia • keratitis • telangiectasias • retinopathy • optic chiasm neuropathy • chronic painful eye • maculopathy • papillopathy • visual field deficits • glaucoma	RT to a vol exposing the eye and orbit	RT coivolgente l'occhio	**RT** = 1 (Yes) AND **Site of RT** = 1.1 (Whole brain), 1.98, 1.99 2.1 Orbit/eye, 2.98, 2.99 50.51, 50.59
			Including TBI	TBI	OR 50.50
			Radioiodine therapy (I-131 ablation therapy)	Terapia ablativa con radioiodio	OR **RT** = Yes AND **Type of RT** = 3 AND **metabolic/radionucleide therapy specify** = 1 (Iodine I131)

Elenco Variabili SurPass dopo implementazione linee guida europee

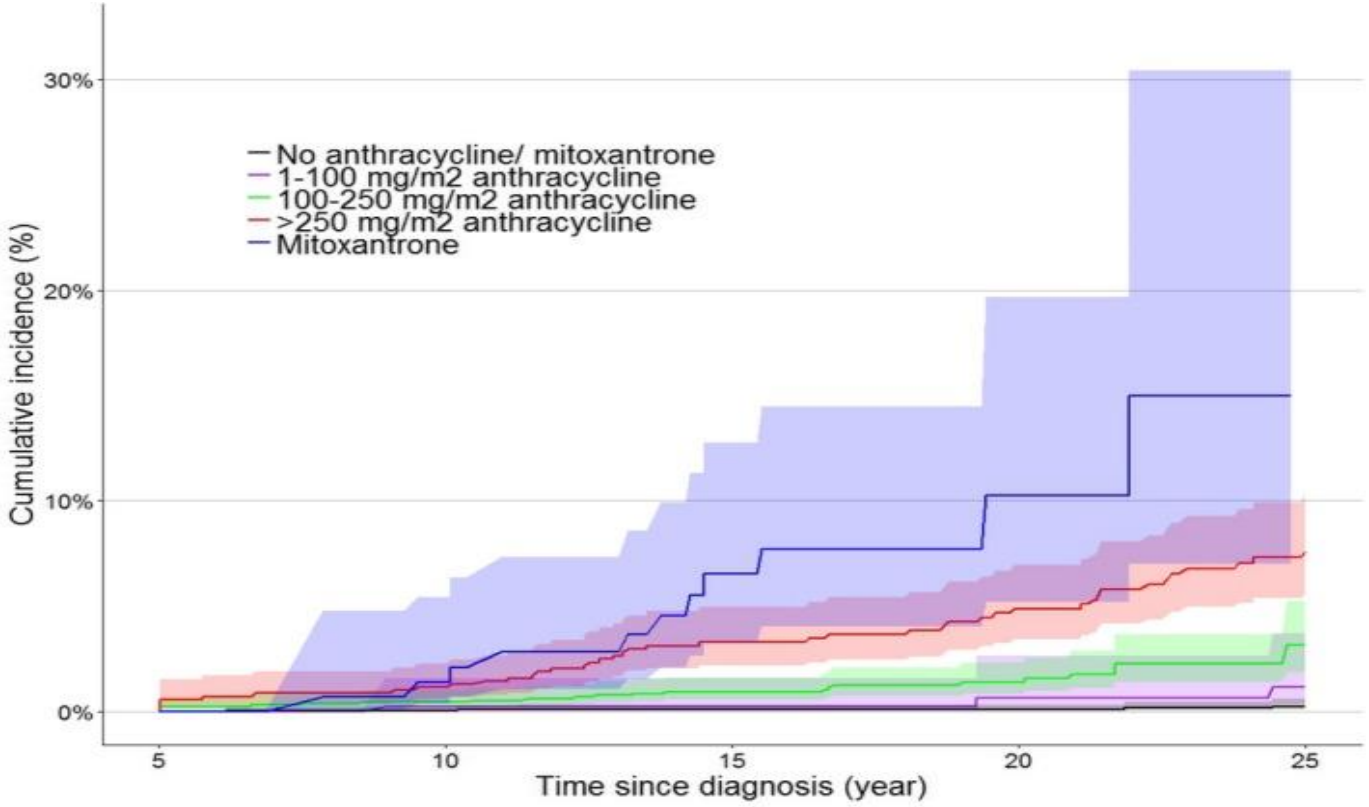


Variables list_TS_PCFU_SurPass_ 2020-July-31_xReport EU - Microsoft Excel

VARIABLE LABEL SurPass	VARIABLE LABEL Surpass in Italian	VARIABLE LABEL PCFU	VARIABLE NAME	TYPE OF FIELD	DATA TYPE	CODING	MANDATORY	COMMENTS SURPASS	COMMENTS PCFU	Variables for SurPass dbase	Variables for PCFU dbase	NOTE
Registration Form												
UPN 101	UPN Mod.1.01		UPN101		number		Yes	Please insert here the "UPN 101" ID number. This is an AIEOP Code to be used by Cineca for pseudonymization of survivors. Will be deleted in the final file to be sent to Castor		Yes	No	
PCFU ID	PCFU ID	CFU ID	To be assigned by DK		number?			Unique Personal Number for the PCFU Study. This field is not reported in the SurPass database and will be manually inserted by IGG	Unique PCFU ID number	No	Yes	
Lastname	Cognome		LASTNAME	textbox	text		Yes	Please insert here the actual lastname of the survivor. This name might be changed (because of marriage, adoption, personal choice) from the one the person had when was diagnosed with cancer (see next field)		Yes	No	
Lastname at diagnosis (if different from th actual one)	Cognome alla diagnosi (se diverso da quello attuale)		LASTNAME1	textbox	text		No	In case that the person has now a different lastname from the one he or she had when was treated for cancer, insert here the lastname of the person at the time of treatment (usually it is the name you find on the clinical record)		Yes	No	
Middlename	Secondo nome		MIDDLENAME	textbox	text		No	Insert here the person's middlename (if any)		Yes	No	
Firstname	Nome di battesimo		FIRSTNAME	textbox	text		Yes	Insert here the person's first (given) name		Yes	No	
Gender	Sesso	Gender	GENDER	select	number	1 => Male 2 => Female 3 => Other	Yes	Please insert "Other" if individuals are neither male or female in gender identity	Please use "other" if individuals are neithe male nor female in gender identity	Yes	Yes	
If other, specify	Se altro, specificare	Gender specification	GENDER_OTH	textbox	text		If GENDER = 3	Describe gender identity	Please specify the gender of the survivor if they prefer to self-identify or if they prefer not to see. Report a transgender history if relevant.	Yes	Yes	
Date of birth	Data di nascita		DOBDT	date	date	dd/mm/yyyy	Yes	Insert the exact date of birth with the dd/mm/yyyy format. **NOTE: In PCFU only the Year of Birth is requested (yyyy)**		Yes	No	
		Year of birth	DOBDT_Y	number	number		Yes	YYYY of birth (automatically generated)	Year of birth in YYYY format			

VariablesList | Radiotherapy sites codes | Hereditary syndromes | Drugs_ATC codes

Dose cumulativa di antraciclinici e rischio di cardiomiopatia



	3064	2845	2244	1686	1263
	451	414	274	221	171
	1351	1261	1022	543	194
	705	639	523	398	280
	146	133	81	25	4

Feijen EAM, J med Heart Ass 2019

Dose equivalenza per cardiomiopatia tardiva di Doxorubicina con Epirubicina e Mitoxantrone

Table 3. Cardiomyopathy HRs and Mean Equivalence Ratios for Various Anthracyclines or Mitoxantrone Relative to Doxorubicin

Exposure	Participants, No.		HR (95% CI)[a]			Ratio (95% CI)	
	Clinical Cardiomyopathy	Dose Information	<150 mg/m²	150-299 mg/m²	≥300 mg/m²	Mean	Linear Dose-Response Model
Daunorubicin	65	4328	1.4 (0.9-2.1)	2.8 (1.7-4.5)	6.0 (3.8-9.3)		
Doxorubicin			1.8 (1.2-2.6)	4.6 (3.3-6.4)	12.6 (9.8-16.3)		
Daunorubicin to doxorubicin ratio			0.8	0.6	0.5	0.6 (0.4-1.0)	0.5 (0.4-0.7)
Epirubicin	9	342	1.9 (0.3-13.7)	2.4 (0.6-9.9)	6.0 (2.6-13.9)		
Doxorubicin			1.5 (0.99-2.2)	4.2 (3.1-5.7)	11.3 (8.8-14.4)		
Epirubicin to doxorubicin ratio			1.3	0.6	0.5	0.8 (0.5-2.8)	0.8 (0.3-1.4)
Idarubicin[b]	5	238	0	3.8 (1.5-9.5)	0		
Doxorubicin			1.4 (0.9-2.1)	4.1 (3.0-5.7)	11.1 (8.6-14.1)		
Idarubicin to doxorubicin ratio			0	0.9	0	NE	NE
Mitoxantrone[c]	19	261	4.2 (1.8-9.9)	4.2 (1.6-11.4)	48.3 (24.2-96.5)		
Doxorubicin			1.5 (1.0-2.3)	4.4 (3.2-6.0)	11.6 (9.1-15.0)		
Mitoxantrone to doxorubicin ratio			2.8	1.0	4.2	10.5 (6.2-19.1)[d]	13.8 (8.0-21.6)[d]

Abbreviations: HRs, hazard ratios; NE, not estimable.

[a] Patient without exposure to the given anthracycline or anthraquinone as referent; models were adjusted for sex, age at diagnosis, exposure to any other anthracycline or mitoxantrone besides the 2 being compared, and stratified by cohort.

[b] Idarubicin doses multiplied by a factor of 5 to facilitate comparability to doxorubicin doses; at a level of less than 150 mg/m², 82 patients had dose information (none with cardiomyopathy); at a level of 300 mg/m² or higher, 28 patients had dose information (none with cardiomyopathy).

[c] Mitoxantrone doses multiplied by a factor of 4 to facilitate comparability to doxorubicin doses.

[d] Multiplied by a conversion factor of 4 (eg, mean ratio of 2.6 × 4 = 10.5).

Feijen EAM, JAMA Oncol. 2019

Tassi di conversione in Doxo equivalenti per il calcolo dose cumulativa antarciclinici (per cardiotossicità)

Tasso di conversione	Doxo	Dauno	Epi	Mitox
Ematologica	1	1	0,64	4
Cardiomiopatia	1	0,5	~0,8	~10

Proposta di modifica x raccomandazioni cardiomioptia

Fattore di rischio	
Antarcicline ≥100-250 mg/m^2	Ogni 5 anni a partire da 2 anni dopo la fine del trattamento cardiotossico
Mitoxantrone ≥10-25 mg/m^2	
Antarcicline ≥250 mg/m2	Ogni 2,5 anni a partire da 2 anni dopo la fine del trattamento cardiotossico
Mitoxantrone ≥25 mg/m^2	

The Follow-up Form (prototype)

- Survivor data
- Summary of the previous follow-up visit (un-modifiable)
- Date of visit
- Update of medical history (display previous data that can be confirmed or modified)
  - Education
  - Work
  - Marital status/offspring
  - Medical …
- Physical exam
  - Anthropometric measures, Tanner
  - …
- Lab tests (empty form)
  - "click" on those done; results are uploaded as pdf files (to be seen by survivor)
- Imaging tests
  - "click" on those done; results are uploaded as pdf files (to be seen by survivor)
- Specialists visits
- Prescriptions
  - Name of drug, schedule, date start, date end (if any)
- Summary of the follow-up visit (free text to be reported at the beginning of next visit)
- **Summary table of chronic conditions (predefined categories)**
- Communications from the survivor between two visits

survivorship PASSPORT

General Coding for Chronic Conditions
(Draft)

categoria	organo	patologia	epoca d'insorgenza (data)	note
cardiovascolare	cuore	cardiomiopatia		
cardiovascolare	cuore	aritmie		
cardiovascolare	cuore	anomalie valvolari		
cardiovascolare	cuore	infarto miocardico		
cardiovascolare	cuore	altro		
cardiovascolare	pericardio	versamento cardiaco		
cardiovascolare	pericardio	pericardite		
cardiovascolare	pericardio	fibrosi del pericardio		
cardiovascolare	pericardio	altro		
cardiovascolare	apparato vascolare (escluso cerebrovascolare???)	patologia carotidea		
cardiovascolare	apparato vascolare (escluso cerebrovascolare???)	stenosi vascolare		
cardiovascolare	apparato vascolare (escluso cerebrovascolare???)	ipertensione		
cardiovascolare	altro			
respiratorio	polmone	sindrome restrittiva		
respiratorio	polmone	altro		
respiratorio	altro			
endocrino e riproduttivo	ipofisi	deficit crescita		
endocrino e riproduttivo	ipofisi	pubertà precoce		
endocrino e riproduttivo	ipofisi	adenomi		
endocrino e riproduttivo	ipofisi	ipotiroidismo centrale		
endocrino e riproduttivo	ipofisi	ipogonadismo ipogonadotropo		
endocrino e riproduttivo	ipofisi	panipopituitarismo		
endocrino e riproduttivo	ipofisi	altro		
endocrino e riproduttivo	pancreas	diabete mellito		
endocrino e riproduttivo	pancreas	altro		
endocrino e riproduttivo	tiroide	ipotiroidismo primitivo		
endocrino e riproduttivo	tiroide	ipertiroidismo		
endocrino e riproduttivo	tiroide	noduli tiroidei		
endocrino e riproduttivo	apparato riproduttivo femminile	amenorrea primaria		
endocrino e riproduttivo	apparato riproduttivo femminile	amenorrea secondaria		

Il ROT

- Migrazione su Piattaforma AIEOP/CINECA
- Nuovo protocollo

Il ROT *Migrazione su Cineca*
Appaiamento dei casi