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Acceptability and feasibility of post-treatment fertility preservation in women previously treated for hematological diseases

Short title: Feasibility of fertility preservation post-treatment

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Data availability statement
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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The authors declare no conflict of interest.
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Authors' contribution
CC, NB and CP contributed to the design and the data analysis All authors contributed to the interpretation of the analysis results –CC, NB and CP wrote the original draft of the letter and incorporated the comments by the co-authors in all subsequent drafts – All authors provided review and edits and approved the final draft of the letter.

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Fertility preservation (FP) is a critical component of medical care for children, adolescents and young adults with hematological diseases undergoing gonadotoxic therapy, given the high survival rates associated with these conditions. In women, the risk of premature ovarian insufficiency (POI) depends on the type and dose of treatment, as well as the age at diagnosis and the initial ovarian reserve (OR). Fertility preservation is most efficient when done prior to treatment (32% and 33% live birth rate after oocyte and ovarian tissue cryopreservation respectively)[1] but it is not always feasible because of disease related factors (eg need for urgent treatment, severe thrombocytopenia or neutropenia, risk of malignant contamination) or patient related factors (poor clinical status, cultural prohibitions) and lack of knowledge, particularly in the early 2000s.[2] Consequently, it is still possible to encounter women in consultation who did not benefit from FP prior to treatment. In such cases, the possibility of performing FP post-treatment should be considered.

Few studies have reported their experience with FP post-treatment, and none have specifically evaluated the feasibility of FP based on prior treatments received.[3–6] Importantly, data that may guide clinicians on when post-treatment FP is feasible, when it can reasonably be forgone, and when referral should ideally occur remain scarce**.** The aim of our single-center retrospective study was to assess ovarian function and the feasibility of oocyte cryopreservation in women already treated for a malignant or non-malignant hematological disease.

In this study, women included between 2013 and 2021, were referred by their hematologist, for the first time, to the fertility preservation consultation localized inside the hematology consultation department, irrespective of any desire for childbearing. Information regarding hematological diagnosis, reason for no anterior FP, treatment history, and post-treatment ovarian function was reviewed from their medical records. Patients were categorized into three groups (G1, G2 and G3) based on their prior treatments: G1 included women who had undergone hematopoietic stem cell transplantation (HSCT), G2 comprised those treated with chemotherapy containing bifunctional alkylating agents (BFAA) without HSCT and G3, women treated with no BFAA-alkylating agents (Table S1). OR was assessed using antral follicular count (AFC) via transvaginal ultrasound and blood hormone assays, including follicle-stimulating hormone (FSH; IU/L) and anti-Müllerian hormone (AMH; ng/mL). Women presenting with amenorrhea lasting more than 4 months and an FSH level> 25 UI/L were classified as having POI. Women still menstruating were categorized as having diminished OR (DOR; AMH<1.2 ng/mL) or normal OR (NOR; AMH>1.2 ng/mL).[7] Based on the treatment received, OR, pregnancy occurrence, and the feasibility of a FP through oocyte vitrification

(OV) following controlled ovarian stimulation (COS), were analyzed for each group. Differences between treatment groups were assessed using Mann-Whitney test for continuous variables and Fisher's exact tests for categorical data. Kaplan-Meier survival analysis estimated cumulative pregnancy rates, with univariate cox models comparing groups. A significance threshold of $p<0.05$ was applied throughout. All statistical analyses were conducted using STATA-18 software (StataCorp LLC, College Station, TX, USA). Ethics approval was granted by the Cochin University Hospital Ethical Review Committee for publications, Paris, France (reference AAA-2023-09016).

Fifty-eight consecutive women were included in this study (G1: n=19, G2: n=32 and G3: n=7), 51 women (87.9%) had malignant hematological conditions, while 7 (12.1%) had severe non-malignant diseases (Table S2). The median age at treatment and FP consultation was 23.5 years (range, 1.0-41.0) and 28.9 years (range, 17.6-42.6) respectively and was not different between the three groups (Table 1). However, G1 patients experienced a significantly longer interval between treatment completion and their first FP consultation ($p<0.001$). Post-treatment ovarian function assessment was available for 48 women (82.7%). In G1, OR was significantly impaired compared to G2+G3 ($p\leq0.001$), consequently, the risk of POI was significantly higher in G1 compared to G2+G3 ($p<0.001$). Age at treatment in G1was statistically higher in women with POI than in those with DOR ($p=0.02$). When comparing G2 and G3, no significant differences were found in hormonal parameters, except for a significantly lower AFC in G2 ($p=0.03$). Two women in G2 were diagnosed with POI, while none in G3. The median cumulative dose of cyclophosphamide received in G2 was 2926 mg/m^2 (range, 1000-7200) (Table 1).

Twenty-one women expressed a child desire following treatment. Thirteen women became pregnant, 10 through natural conception, 1 through assisted reproductive technology (ART) and 2 through oocytes donation. Ten live births were achieved (Table 1). Natural pregnancies (NP) occurred in 9 women in G2 (9/32) and 1 in G3 (1/7), median age at pregnancy was 30.8 years (range, 27.5-36.7). Three women in G2 experienced a second NP (Table S2). The cumulative rate of NP in the overall population reached 35% by 7.5 years post-treatment (Figure 1A). In G2 and G3, this rate reached or exceeded 60% at 7.5 years, whereas G1 showed a significantly lower cumulative rate of 10% (Figure 1B) ($p<0.05$). Women with lymphoma, who received cumulative cyclophosphamide doses up to 7.200 mg/m², showed the highest pregnancy rates, while those with non-malignant conditions had the lowest (Figure 1C). Among the 21 women (36.2%) who had expressed a desire to have children, 8 (38.1%) got pregnant. Among the five other pregnant women (13.5%) who did not wish to have children, two underwent elective

abortions. FP was considered for 30 women (62.5%) who had an OR deemed suitable for COS. Eleven women (36.7%) proceeded with the procedure, while 19 (63.3%) declined the offer. FP was performed in 2/6, 6/19 and 3/5 women in G1, G2 and G3 respectively. The median age at OV was 24.5 (range, 19.3-34.3). In G2, the cumulative dose of cyclophosphamide received was 2500 mg/m2 (1000-6700). The median number of vitrified oocytes was 6 (range, 0-20). G1 patients exhibited a notably low number of retrieved oocytes (n=2), while G2-G3 patients demonstrated broader variability, with 2 to 20 vitrified oocytes per women (Table 2).

To our knowledge, this study represents the largest series evaluating NP and the feasibility of FP post-treatment in women with hematological diseases, based on individualized treatment history. In our overall cohort, 17.2% of women achieved a NP, which is lower than the 38% reported by Chow et al.[8] However, when considering only women who had expressed a child desire, 38.1% achieved a NP.

By stratifying our study population into three treatment groups, we may provide practical guidance for clinicians regarding which patients may benefit from post-treatment FP.

As expected**,** women in G1 exhibited the lowest probability of NP [9] and the poorest response to COS, underscoring the critical importance of performing FP prior to treatment whenever possible. Nevertheless, this should be qualified by a recent study by Sockel et al., reporting a 3.4% pregnancy rate after HSCT, with 72% natural conceptions. Consistent with their findings, we also confirmed that age at treatment is a determinant of ovarian reserve.[10] In G2, AMH levels and prior exposure to high dose of cyclophosphamide did not appear to correlate with the likelihood of natural pregnancy before 30 years old, as previously reported.[8,11] Six women in G2 with altered OR became pregnant, and 3 of them experienced a second natural pregnancy. This observation aligns with the findings of Chow et al, who reported no correlation between cumulative cyclophosphamide dose, up to 11 g/m^2, and pregnancy outcome.[8] In G3, hormonal profiles were close to normal, consistent with the findings of van den Berg et al.[12]

Few studies have reported on COS in women after cancer treatment, either during ART protocols for embryo or OV.[6,13,14] The median oocyte yield number in our cohort was comparative to a recent study[6] and reflects our choice to proceed with COS despite DOR, due to the fertility preservation context. Importantly, no difference was observed in the number of retrieved oocytes between G2 and G3.These results suggest that post-treatment FP should not be dismissed in women treated with BFAA without HSCT, even in the presence of DOR and

that repeated COS cycles may be discussed to optimize oocyte yield, [4,6,15] as implemented in three women within our cohort.

Recently, Miquel et al reported a promising cumulative live birth rate of 38% from oocytes collected after cancer treatment[5], highlighting the value of post-treatment FP. However, even when FP was offered, many women chose not to undergo the procedure, as previously reported by Benedict et al.[16]

From a practical standpoint, ovarian function assessment and counseling should be systematically proposed within 1–2 years after completion of chemotherapy.[15] Women treated with HSCT are poor candidates for post-treatment FP. These women should be counselled accordingly and referred, whenever possible, for FP before HSCT. In contrast, women treated with BFAA without HSCT have a lower risk of compromised fertility and a potential for NP and successful oocyte retrieval, highlighting that fertility potential may persist despite altered OR. They should then receive individualized counselling regarding reproductive options, regardless of hormonal profile. Contraceptive advice should also be provided when there is no desire for pregnancy (cf. 2 elective abortions in our series). Women treated with non-alkylating agents are suitable candidates for post-treatment FP, or annual monitoring of ovarian function for those considering delaying FP.

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Table 1. Characteristics of women at post-treatment fertility preservation consultation according to the type of treatment received

	General Population	G1	G2	G3	p (G1/G2+G3)	p (G2 /G3)
n (%)	58 (100.0)	19 (32.7)	32(55.2)	7 (12.1)		
Median age at TTT (years) [range]	23.5 [1.0-41.0]	21.0 [1.0-36.6]	23.0 [5-41]	29.0 [14.0-33.2]	0.308	0.323
Median age at HSCT (years) [range]		25.8 [2.7-37.4]	NA	NA		
Allo-HSCT n (%)	15 (25.8)	15 (78.9)	0	0		
MAC/RIC regimen n (%)	9 (15.5)/6 (10.3)	9 (60.0)/6 (40.0)				
Auto-HSCT n (%)	4(6.9)	4 (21.1)	0	0		
Total cyclophosphamide dose (mg/m²)	NA	NA	2926 [1000-7200]	0		
Malignant hematological diseases n (%)	51 (87.9)	12 (63.2)	32 (100.0)	7 (100.0)		
B-ALL	11 (19.0)	2 (10.5)	9 (28.1)	0		
T-ALL	7 (12.1)	1 (5.3)	6 (18.8)	0		
AML	9 (15.5)	4 (15.8)	0	5 (71.4)		
CML	1 (1.7)	1 (5.3)	0	0		
HL	16 (27.6)	1 (5.3)	13 (40.6)	2 (28.6)		
NHL	7 (12.1)	3 (21.0)	4 (12.5)	0		
Non-malignant hematological diseases n (%)	7 (12.1)	7 (36.8)				
Bone marrow failure	2 (3.4)	2 (10.5)	0	0		
Sickle cell disease	2 (3.4)	2 (10.5)	0	0		
Fanconi Anemia	3 (5.2)	3 (15.8)	0	0		
Median age at FP consultation	28.9 [17.6-42.6]	29.8 [17.5-40.9]	27.7 [17.9-42.6]	29.9 [17.7-35.1]	0.502	0.797
Median time from TTT to FP consultation (years) [range]	3.2 [0.2-24.8]	5.9 [0.8-24.8]	2.0 [0.15-16.3]	1.6 [0.6-3.4]	<0.001	0.534
Ovarian reserve (OR) n (%)	48 (82.7)	16 (84.2)	27 (84.4)	5 (71.4)		
Median age at OR evaluation year [range]	28.3 [14.6-41.2]	28.2 [15.4-41.2]	27.9 [18.7-38.9]	28.2 [14.6-32.9]	0.831	0.925
Median time from TTT to OR evaluation	3.3 [0.3-24.8]	5.9 [1.0-24.8]	1.9 [0.3-7.5]	1.4 [0.3-2.8]	<0.001	0.327
Median hormonal levels [range] FSH (UI/L)	9.6 [3.3-160.8]	42.5 [4.8-160.8]	7.8 [3.3-98.5]	6.7 [3.5-11.8]	<0.01	0.132
AMH ng/ml	0.50 [0.01-13.20]	0.07 [0.01-1.00]	1.00 [0.05-7.13]	2.50 [0.11-13.20]	<0.001	0.259

Antral follicular count n (%)	39 (67.2)	11 (57.9)	24 (75)	4 (57.1)		
Median follicle number (n; range)	7 [0-40]	4 [0-7]	9 [1-25]	20 [11-40]	<0.001	0.03
Ovarian status n (%)						
NOR	13 (27.1)	0	10 (37.0)	3 (60.0)		
DOR	24 (50.0)	7 (43.8)	15 (55.6)	2 (40.0)		
POI	11 (22.9)	9 (56.2)	2 (7.4)	0	<0.001	0.737
Childbearing desire n (%)	21(36.2)	9 (47.4)	9 (28.1)	3 (42.8)		
Total pregnancy n	13	1*	9+1*	1+1[#]		
Natural pregnancy n (%=n/total population)	10 (17.2)	0	9 (28.1)	1 (14.3)		
Lives Birth	10	1	7	2		
Elective abortion	2		2			
Ectopic pregnancy	1		1			

AMH: anti-Müllerian hormone; AML: acute myeloblastic leukemia; B-ALL: B-acute lymphoblastic leukemia; CML: chronic myeloid leukemia; DOR: diminished ovarian reserve; FP: fertility preservation, FSH: follicle-stimulating hormone; G1: Hematopoietic stem cell transplantation; G2: Chemotherapy with bifunctional alkylating agents without HSCT; G3: Chemotherapy with no bifunctional alkylating agents; HL: Hodgkin lymphoma; HSCT: hematopoietic stem cell transplantation; LH: luteinizing hormone; MAC: myeloablative conditioning regimen; NA: not applicable; NHL: non-Hodgkin lymphoma; NOR: normal ovarian reserve; POI: premature ovarian insufficiency; RIC: reduced intensity conditioning regimen; T-ALL: T-acute lymphoblastic leukemia; TTT: treatment.* oocyte donation; [#] assisted reproductive technology.

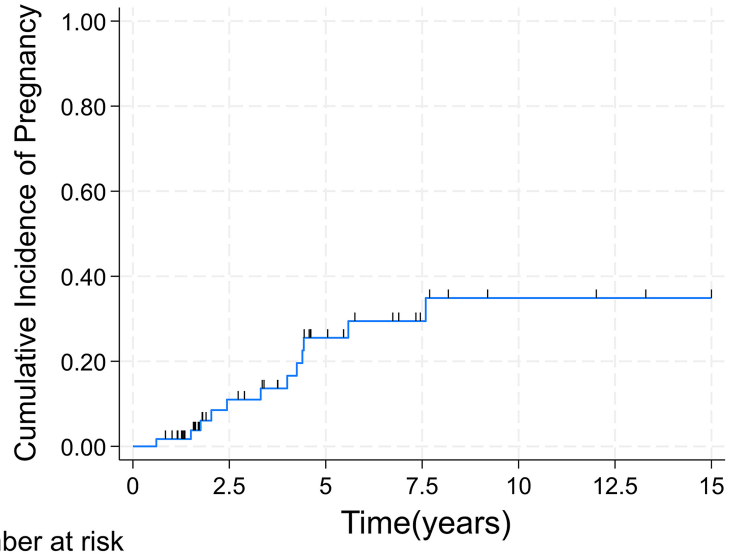
Table 2. Characteristics of women undergoing fertility preservation post treatment and results of fertility preservation

Hematological disease	TTT group	Age at TTT (years)	Time since the end of TTT (years)	CP dose (mg/m^2)	Age at COS (years)	FSH UI/L	LH UI/L	E2 pmol/L	AMH ng/mL	AFC	Number of COS cycles	Cumulative number of vitrified oocytes
Median [range]		16.0 [4.0-29.2]	7.7 [1.6-14.3]	2500 [1000-6700]	24.5 [19.3-34.3]	6.8 [3.3-18.2]	5.2 [1.8-31.1]	146.8 [25.0-651.0]	1.1 [0.1-5.0]	11 [4-28]	1 [1-3]	6 [0-20]
Fanconi A	**G1**	6.0	14.3	1000	20.4	6.8	4.2	94	1.0	7	1	2
CML	**G1**	4.0	12.8	6700	19.5	4.8	8.2	462	0.1	4	1	0
B-ALL	**G2**	16.0	1.6	1000	21.1	9.7	5.6	147	1.8	11	1	3
B-ALL	**G2**	15.9	8.3	1000	27.1	12.9	5.2	169	0.3	9	2	10
B-ALL	**G2**	15.6	7.2	1000	23.6	6.8	5.4	106	1.3	21	1	6
T-ALL	**G2**	15.0	2.1	4000	19.3	18.2	31.1	651	1.1	4	1	4
T-ALL	**G2**	19.0	8.4	5250	29.7	7.4	4.4	121	1.0	11	3	18
NHL	**G2**	26.4	7.7	4500	34.3	3.3	1.8	497	1.7	11	1	9
AML	**G3**	22.3	2.0	0	24.5	11.8	3.6	25	5.0	28	1	20
AML	**G3**	29.0	4.0	0	33.4	3.6	3.9	25	4.4	7	1	2
HL	**G3**	29.2	2.7	0	32.3	6.8	5.6	172	0.9	11	2	6

AFC: antral follicular count; AMH: anti-Müllerian hormone; AML: acute myeloblastic leukemia; B-ALL: B-acute lymphoblastic leukemia-B; CML: chronic myeloid leukemia; COS: controlled ovarian stimulation; CP: cyclophosphamide; E2: Estradiol; Fanconi A: Fanconi Anemia; FSH: follicle-stimulating hormone ; G1: Hematological stem cell transplantation; G2: Chemotherapy with bifunctional alkylating agents; G3: Chemotherapy with no bifunctional alkylating agents; HL: Hodgkin lymphoma; LH: luteinizing hormone; NHD: non-Hodgkin lymphoma; T-ALL: T-acute lymphoblastic leukemia; TTT: treatment.

Figure 1. Cumulative incidence of pregnancy after treatment completion.
A) Cumulative incidence of pregnancy in the overall population, B) Cumulative incidence of pregnancy according to prior treatment, C) Cumulative incidence of pregnancy according to diagnosis.

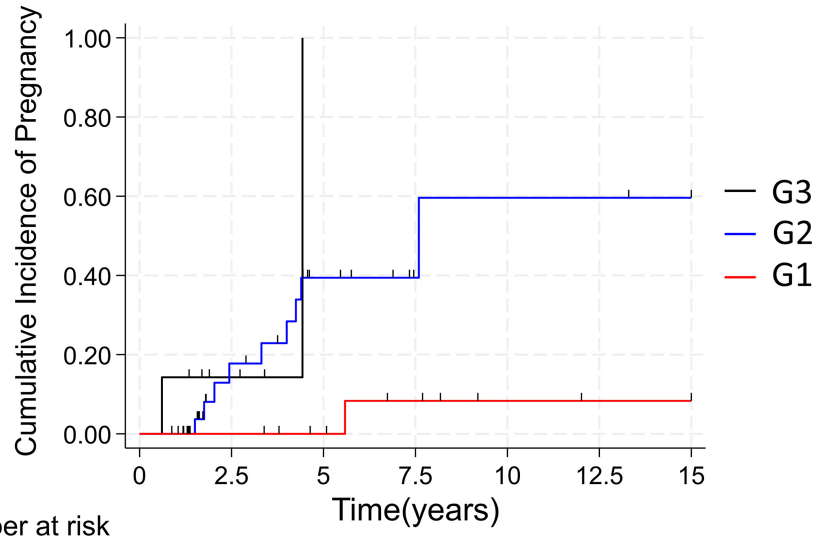
A)



Number at risk

	58	36	21	13	9	8	7

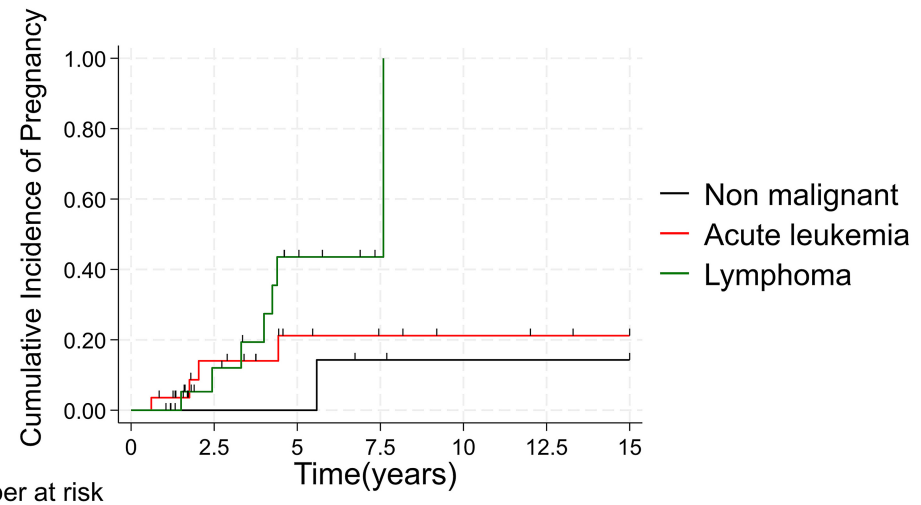
B)



Number at risk

No alkyl	7	3	0	0	0	0	0
Alkyl	32	17	8	3	2	2	1
Graft	19	16	13	10	7	6	6

C)



Number at risk

Non malignant	7	7	7	5	4	4	4
Acute leukemia	28	16	9	7	5	4	3
Lymphoma	23	13	5	1	0	0	0

Supplemental Table 1. Examples of mono and bifunctional alkylating agents (from Goodman & Gilman's The Pharmacological Basis of Therapeutics, 12th edition, 2011)

Monofunctional alkylating agents	Bifunctionnal alkylating agents
Triazenes / Hydrazines :Dacarbazine, Temozolomide…	Nitrosoureas: Carmustine (BCNU), Lomustine (CCNU), Fotemustine, Nitrogen mustards / Oxazaphosphorines: Cyclophosphamide, Ifosfamide, Melphalan, Chlorambucil, Bendamustine Alkyl sulfonates: Busulfan Ethylene imines / Aziridines: Thiotepa, Altretamine…

Supplemental Table 2. Detailed studied population

TTT group	Diseases	Age at TTT (years)	HSCT	Received TTT	CP dose received (mg/m2)	Reason for no FP preTTT	Ovarian status post-TTT	FP post-TTT	Cumulative oocyte pick-up	Pregnancy post-TTT
G1	ABMF	35.0	allograft	RIC		CC	NA	NO		After OD
G1	IBMF	15.0	allograft	RIC		CC	DOR	NO		
G1	SCD	6.0	allograft	MAC		CC	POI	NO		
G1	SCD	4.0	allograft	MAC		CC	DOR	NO		
G1	FA	30.0	allograft	RIC		CC	DOR	NO		
G1	FA	6.0	allograft	RIC		ELGT	DOR	YES	2	
G1	FA	9.0	allograft	RIC		CC	POI	NO		
G1	B-ALL	8.0	allograft	MAC		CC	POI	NO		
G1	B-ALL	30.5	allograft	MAC		CC	NA	NO		
G1	T-ALL	33.3	allograft	RIC		ETT	POI	NO		
G1	AML	1.0	allograft	MAC		NA/NI	DOR	NO		
G1	AML	30.6	allograft	MAC		NA/NI	NA	NO		
G1	AML	26.5	autograft	MAC		ETT	POI	NO		
G1	AML	10.0	allograft	MAC		ETT	DOR	NO		
G1	CML	4.0	allograft	MAC		NA/NI	DOR	YES	0	
G1	HL	25.0	autograft	MAC		ETT	POI	NO		
G1	NHL	36.6	allograft	MAC		CC	POI	NO		
G1	NHL	21.0	autograft	MAC		NA/NI	POI	NO		
G1	NHL	25.4	autograft	MAC		ETT	POI	NO		
G2	B-ALL	15.9		FRALLE-B[1]	1000	ELGT	DOR	YES	10	
G2	B-ALL	6.0		FRALLE-B	1000	ELGT	NA	NO		
G2	B-ALL	5.0		FRALLE-B	1000	ELGT	NOR	NO		
G2	B-ALL	13.6		FRALLE-B	1000	ELGT	NA	NO		NP
G2	B-ALL	15.6		FRALLE-B	1000	ELGT	NOR	YES	18	
G2	B-ALL	15.3		FRALLE-B	1000	ELGT	NOR	NO		
G2	B-ALL	21.0		FRALLE-B	3000	ELGT	NOR	NO		
G2	B-ALL	16.0		FRALLE-B	1000	ELGT	NOR	YES	3	
G2	B-ALL	11.0		EORTC 58591[2]	4000	ELGT	NA	NO		

G2	T-ALL	15.0		FRALLE-T[1]	4000	ELGT	DOR	YES	4	
G2	T-ALL	23.0		GRAALL-2014[3]	4600	ELGT	NOR	NO		NP
G2	T-ALL	22.5		GRAALL-2014	4600	ELGT	NOR	NO		
G2	T-ALL	19.0		LL03[4]	5250	ETT	DOR	YES	6	
G2	T-ALL	26.0		GRAALL-2014	6000	ETT	DOR	NO		NP
G2	T-ALL	19.7		FRALLE-T	4000	ETT	DOR	NO		
G2	HL	24.0		BEACOPP+ABVD	1300	ELGT	DOR	NO		
G2	HL	24.6		BEACOPP+ABVD	3600	ELGT	DOR	NO		NP*
G2	HL	22.9		BEACOPP	7200	ETT	POI	NO		NP*
G2	HL	25.6		BEACOPP+ABVD	2400	ELGT	DOR	NO		NP
G2	HL	27.0		BEACOPP	3900	ELGT	DOR	NO		NP
G2	HL	26.0		BEACOPP	3600	NA/NI	DOR	NO		
G2	HL	24.0		COPDAC+ABVD	4000	NA/NI	NA	NO		
G2	HL	32.0		BEACOPP+ABVD	1300	ELGT	DOR	NO		After OD
G2	HL	30.0		BEACOPP+ABVD	1300	ELGT	DOR	NO		
G2	HL	33.8		BEACOPP	1200	ELGT	DOR	NO		NP*
G2	HL	17.9		OEPA+COPDAC	2000	ELGT	NOR	NO		
G2	HL	33.5		BEACOPP+ABVD	1300	ELGT	DOR	NO		
G2	HL	41.0		BEACOPP+ABVD	2600	NA/NI	NA	NO		
G2	NHL	26.4		R-CHOP	4500	ELGT	NOR	YES	9	
G2	NHL	30.0		R-CHOP	4500	ELGT	NOR	NO		NP
G2	NHL	18.0		Euro-LB[5]	2000	ELGT	DOR	NO		
G2	NHL	38.2		R-CHOP	4500	ELGT	POI	NO		
G3	AML	33.2		DAUNO-ARA-C	0	ELGT	NA	NO		
G3	AML	29.0		DAUNO-ARA-C	0	ELGT	NA	YES	2	NP
G3	AML	14.0		ELAM-02[6]	0	ELGT	DOR	NO		
G3	PAL	30.0		ATRA+ATO	0	CC	NOR	NO		After ART
G3	AML	22.3		DAUNO-HDAC	0	ELGT	NOR	YES	20	
G3	HL	24.0		ABVD	0	ELGT	NOR	NO		
G3	HL	29.2		ABVD	0	ELGT	DOR	YES		

ABMF: acquired bone marrow failure; ABVD: doxorubicin-bleomycin-vinblastine-dacarbazine; AML: acute myeloblastic leukemia; ARA-C: cytarabine; ART: assisted reproductive technology; ATO: Arsenic TriOxyde; ATRA: All-Trans Retinoic Acid; B-ALL: B-acute lymphoblastic leukemia; BEACOPP: bleomycin-etoposide-doxorubicin-cyclophosphamide-vincristine-procarbazine-prednisone; CC: clinical conditions; CML: chronic myeloid leukemia; COPDAC: cyclophosphamide-vincristine-prednisone-dacarbazine; CP: cyclophosphamide; DAUNO: daunorubicin; DOR: diminished ovarian reserve; ELGT: estimated low gonadotoxicity; ETT: emergency to treatment; FA: Fanconi anemia; FP: fertility preservation; G1: Hematopoietic stem cell transplantation; G2: Chemotherapy with bifunctional alkylating agents; G3: Chemotherapy with no bifunctional alkylating agents;

HDAC: High dose cytarabine; HL: Hodgkin lymphoma; IBMF: inherited bone marrow failure; MAC: myeloablative conditioning regimen; NA : not available; NI: no information; NHL: non-Hodgkin lymphoma; NOR: normal ovarian reserve; NP: natural pregnancy; OD: oocyte donation; OEPA: vincristine-etoposide-prednisone-doxorubicin;
POI: premature ovarian insufficiency; PAL: promyelocytic leukemia; R-CHOP: rituximab-cyclophosphamide-adriamycin-vincristine-prednisone; RIC: reduced intensity conditioning regimen; SCD: sickle cell disease; T-ALL: T-acute lymphoblastic leukemia; TTT: treatment. * >1 natural pregnancy.

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