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723. Allogeneic Transplantation: Long-term Follow-up and Disease Recurrence

# CNS Prophylaxis in Adult ALL Patients after Stem Cell Transplantation: An EBMT Survey on General Practice

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Table 1 Summary of results for i.L. prophylaxis and cranial irradiation

Country	CNS prophylaxis (i.L.)				Cranial irradiation			
	n	%	n	%	n	%	n	%
ALL	102	100	102	100	102	100	102	100
AML	102	100	102	100	102	100	102	100
MDS	102	100	102	100	102	100	102	100
MPN	102	100	102	100	102	100	102	100
CMML	102	100	102	100	102	100	102	100
CMML2	102	100	102	100	102	100	102	100
CMML3	102	100	102	100	102	100	102	100
CMML4	102	100	102	100	102	100	102	100
CMML5	102	100	102	100	102	100	102	100
CMML6	102	100	102	100	102	100	102	100
CMML7	102	100	102	100	102	100	102	100
CMML8	102	100	102	100	102	100	102	100
CMML9	102	100	102	100	102	100	102	100
CMML10	102	100	102	100	102	100	102	100
CMML11	102	100	102	100	102	100	102	100
CMML12	102	100	102	100	102	100	102	100
CMML13	102	100	102	100	102	100	102	100
CMML14	102	100	102	100	102	100	102	100
CMML15	102	100	102	100	102	100	102	100
CMML16	102	100	102	100	102	100	102	100
CMML17	102	100	102	100	102	100	102	100
CMML18	102	100	102	100	102	100	102	100
CMML19	102	100	102	100	102	100	102	100
CMML20	102	100	102	100	102	100	102	100
CMML21	102	100	102	100	102	100	102	100
CMML22	102	100	102	100	102	100	102	100
CMML23	102	100	102	100	102	100	102	100
CMML24	102	100	102	100	102	100	102	100
CMML25	102	100	102	100	102	100	102	100
CMML26	102	100	102	100	102	100	102	100
CMML27	102	100	102	100	102	100	102	100
CMML28	102	100	102	100	102	100	102	100
CMML29	102	100	102	100	102	100	102	100
CMML30	102	100	102	100	102	100	102	100
CMML31	102	100	102	100	102	100	102	100
CMML32	102	100	102	100	102	100	102	100
CMML33	102	100	102	100	102	100	102	100
CMML34	102	100	102	100	102	100	102	100
CMML35	102	100	102	100	102	100	102	100
CMML36	102	100	102	100	102	100	102	100
CMML37	102	100	102	100	102	100	102	100
CMML38	102	100	102	100	102	100	102	100
CMML39	102	100	102	100	102	100	102	100
CMML40	102	100	102	100	102	100	102	100
CMML41	102	100	102	100	102	100	102	100
CMML42	102	100	102	100	102	100	102	100
CMML43	102	100	102	100	102	100	102	100
CMML44	102	100	102	100	102	100	102	100
CMML45	102	100	102	100	102	100	102	100
CMML46	102	100	102	100	102	100	102	100
CMML47	102	100	102	100	102	100	102	100
CMML48	102	100	102	100	102	100	102	100
CMML49	102	100	102	100	102	100	102	100
CMML50	102	100	102	100	102	100	102	100
CMML51	102	100	102	100	102	100	102	100
CMML52	102	100	102	100	102	100	102	100
CMML53	102	100	102	100	102	100	102	100
CMML54	102	100	102	100	102	100	102	100
CMML55	102	100	102	100	102	100	102	100
CMML56	102	100	102	100	102	100	102	100
CMML57	102	100	102	100	102	100	102	100
CMML58	102	100	102	100	102	100	102	100
CMML59	102	100	102	100	102	100	102	100
CMML60	102	100	102	100	102	100	102	100
CMML61	102	100	102	100	102	100	102	100
CMML62	102	100	102	100	102	100	102	100
CMML63	102	100	102	100	102	100	102	100
CMML64	102	100	102	100	102	100	102	100
CMML65	102	100	102	100	102	100	102	100
CMML66	102	100	102	100	102	100	102	100
CMML67	102	100	102	100	102	100	102	100
CMML68	102	100	102	100	102	100	102	100
CMML69	102	100	102	100	102	100	102	100
CMML70	102	100	102	100	102	100	102	100
CMML71	102	100	102	100	102	100	102	100
CMML72	102	100	102	100	102	100	102	100
CMML73	102	100	102	100	102	100	102	100
CMML74	102	100	102	100	102	100	102	100
CMML75	102	100	102	100	102	100	102	100
CMML76	102	100	102	100	102	100	102	100
CMML77	102	100	102	100	102	100	102	100
CMML78	102	100	102	100	102	100	102	100
CMML79	102	100	102	100	102	100	102	100
CMML80	102	100	102	100	102	100	102	100
CMML81	102	100	102	100	102	100	102	100
CMML82	102	100	102	100	102	100	102	100
CMML83	102	100	102	100	102	100	102	100
CMML84	102	100	102	100	102	100	102	100
CMML85	102	100	102	100	102	100	102	100
CMML86	102	100	102	100	102	100	102	100
CMML87	102	100	102	100	102	100	102	100
CMML88	102	100	102	100	102	100	102	100
CMML89	102	100	102	100	102	100	102	100
CMML90	102	100	102	100	102	100	102	100
CMML91	102	100	102	100	102	100	102	100
CMML92	102	100	102	100	102	100	102	100
CMML93	102	100	102	100	102	100	102	100
CMML94	102	100	102	100	102	100	102	100
CMML95	102	100	102	100	102	100	102	100
CMML96	102	100	102	100	102	100	102	100
CMML97	102	100	102	100	102	100	102	100
CMML98	102	100	102	100	102	100	102	100
CMML99	102	100	102	100	102	100	102	100
CMML100	102	100	102	100	102	100	102	100

CNS: central nervous system, TBI: Total body irradiation, i.L.: Intrathecal, NA: not available

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Figure 1.

## Introduction

Allogeneic hematopoietic stem cell transplantation (HSCT) is an effective treatment for acute lymphoblastic leukemia (ALL) resulting in long-term remission.

Despite advances in therapy, disease progression remains the major cause of mortality following HSCT accounting for 20-50% of all deaths. The central nervous system (CNS) is the most common extra-medullary site of disease progression after transplant in ALL.

The established practice of CNS prophylaxis for ALL has largely been modeled in the pediatric population, given the higher incidence of ALL in this age group compared with adults.

Although the use of CNS prophylaxis as part of the upfront treatment for ALL has led to significant decreases in CNS relapse and improved outcomes overall, the routine use of post-HSCT prophylactic CNS therapy as a strategy to prevent CNS relapse after transplant in adult patients is still controversial. Studies that utilized post-HSCT CNS prophylaxis have reported disparate results and there is no generalized consensus regarding the use of post-transplant CNS prophylaxis to prevent relapse.

## Methods

In order to assess the current practice of post-HSCT prophylactic CNS therapy in preventing CNS relapse in ALL patients, we carried out a survey among EBMT centres to describe intrathecal (i.t.) prophylaxis or irradiation in HSCT for ALL in both patients with or without CNS manifestations at any time of disease (first or second complete remission [CR1, CR2] and relapsed/refractory [R/R] ALL).

EBMT centres were asked whether they usually give i.t. prophylaxis or cranial irradiation before and after HSCT, and which drugs they use.

## Results

Of 410 invited centres, 55 (13%) replied to the survey. Tables 1 shows the number of centres which use i.t. prophylaxis or cranial irradiation. Most of the 55 centres used both pre-and post i.t. prophylaxis and triple prophylaxis (steroids, cytarabine [AraC] and methotrexate [MTX]) was the most frequently adopted.

As expected in the pre-transplant phase, almost 70% of centres use i.t. chemotherapy irrespective of the phase of the disease or of the use of total body irradiation (TBI) as conditioning regimen. In the post-transplant phase, the rate of i.t. prophylaxis varies according to disease phase, TBI use, and history of CNS involvement pre HSCT.

In patients w/o history of CNS involvement in CR1, i.t. prophylaxis is given in 23.6% and 21.5% (with or w/o TBI use, respectively). Notably in CR2 pts, i.t. prophylaxis is given in 20% of cases if the conditioning regimen includes TBI, and in 74.5% of cases if TBI is not used; 32.7% and 46.9% R/R pts (with or without TBI use, respectively) are given i.t. prophylaxis.

In the setting of patients with history of CNS involvement in CR1, i.t. prophylaxis is given in 30.9% and 38.2% (with or without TBI use, respectively); in CR2 pts, i.t. prophylaxis is given in 38.9% of cases if the conditioning regimen does not include TBI, and in 29.1% of cases if TBI is used; 38.9% and 45.3% R/R pts (with or without TBI use, respectively) are given i.t. prophylaxis.

Pre-transplant cranial irradiation is planned in less than 10% of centres in CR1 and CR2 patients without CNS involvement, irrespective of the use of TBI in the conditioning regimen, while it is used in 22.4% and 25% of patients with R/R disease with or without TBI use for transplant, respectively. In the setting of patients with CNS involvement, among those in CR1 and CR2, approximately 30% receive pre-transplant cranial irradiation irrespective of TBI use, while 32.7% and 34.6% of patients receive cranial irradiation (with or without TBI use, respectively). Its use after transplant is uncommon irrespective of disease status at treatment.

## Conclusions

CR2 pts (without CNS involvement) seem to be at higher risk of CNS relapse if TBI is not included in the conditioning regimen.

R/R pts are always considered at higher risk for CNS relapse if TBI is not included in the conditioning regimen.

Cranial irradiation before treatment is used in almost 1 out of 3 pts with CNS involvement despite the use of TBI as the conditioning regimen, and 1 out of 4 R/R pts without CNS involvement at transplant.

The rate of cranial irradiation after transplant is extremely low, irrespective of disease status, previous CNS involvement or TBI use.

In conclusion, the use of i.t. prophylaxis after HSCT in patients with or without CNS involvement is variable among European transplant centres, also in the era of novel therapies for patients with ALL.

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