Tidsskriftet Tidsskrift for Den norske legeforening

Allogeneic stem cell transplantation for acute myeloid leukaemia 2005–22

ORIGINAL ARTICLE

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Background

Allogeneic stem cell transplantation is the only curative treatment for various blood and bone marrow disorders. The purpose of this study is to describe Norway's use of allogeneic stem cell transplantation to treat acute myeloid leukaemia (AML) and to investigate any potential differences between the four regional health authorities.

Material and method

In the period 1 January 2005 to 31 December 2022, a total of 2979 people were diagnosed with AML in Norway. We identified age, remission status, donor characteristics, survival and transplant-related mortality among the patients who underwent allogeneic stem cell transplantation.

Results

During the study period, 674 out of 2979 patients (22.6 %) diagnosed with AML underwent allogeneic stem cell transplantation. This number increased over time, from 14 transplants in 2005 to 67 in 2020. Treatment outcomes progressively improved: five-year survival increased from 48 % in the period 2005–10 to 63 % in the period 2017–22. The median age of patients from the Central Norway Regional Health Authority (48 years) and Western Norway Regional Health Authority (50 years) was lower than that of patients from the South-Eastern Norway Regional Health Authority (54 years) and Northern Norway Regional Health Authority (60 years). There were no differences between the regional health authorities in terms of gender, remission status or use of related and unrelated donors.

Interpretation

Allogeneic stem cell transplantation is now a central component of treatment for AML. A steadily increasing number of patients are undergoing allogeneic stem cell transplantation with no observed decline in treatment outcomes.

Main findings

A total of 674 out of 2979 (22.6 %) patients diagnosed with acute myeloid leukaemia during the study period underwent allogeneic stem cell transplantation.

The number of stem cell transplants performed to treat acute myeloid leukaemia increased steadily, from 14 in 2005 to 67 in 2020. Five-year survival increased from 48 % in the period 2005–10 to 63 % in the period 2017–22.

Each year, 150 to 200 people are diagnosed with acute myeloid leukaemia (AML) in Norway (1). Most patients receiving curative treatment achieve complete remission with intensive chemotherapy, but many relapse if chemotherapy is the only treatment given (2, 3). Allogeneic stem cell transplantation has reduced the risk of relapse by more than 60 % compared to intensive chemotherapy alone (3) and represents the best curative treatment option for most patients.

The number of allogeneic stem cell transplants is increasing, and AML is now the most common indication for this treatment, both in Norway and globally (4, 5). However, the risk of transplant-related mortality diminishes the survival benefit associated with the strong antileukemic effect of the procedure, thereby reducing the pool of eligible patients. Reduced-intensity conditioning with less toxicity and the use of antithymocyte globulin to prevent graft-versus-host disease have led to a significant reduction in treatment-related mortality without increasing the risk of relapse. As a result, transplantation can now be offered to older patients and patients with comorbidities (3, 4), including patients over 70 years of age (4).

Allogeneic stem cell transplantation is a multi-regional treatment service. The Norwegian Ministry of Health and Care Services established national and multi-regional treatment services in 2010 (6). A multi-regional treatment service is provided by two health trusts situated in separate regional health authorities, based on the principle of equal access for all patients regardless of where they live in the country.

Despite widespread agreement on its potential benefits, it is globally recognised that many patients do not have access to this treatment (5). The purpose of our study was to describe the extent to which allogeneic stem cell transplantation is used to treat AML in Norway, and whether this differs between the regional health authorities.

Material and method

This retrospective study included all adult patients with AML who underwent allogeneic stem cell transplantation at Oslo University Hospital between 1 January 2005 and 31 December 2022, and at Haukeland University Hospital between 1 January 2006 and 31 December 2022. In Norway, allogeneic stem cell transplantation is only performed at these two hospitals as part of a multi-regional treatment service. Data were collected on age, gender, disease stage, date of transplantation, donor characteristics, survival and the patients' regional health authority. These data were obtained from the departments' quality registries. Patients transplanted at Oslo University Hospital have been included in previously published studies on the full scope of stem cell transplantation at Oslo University Hospital (2, 4, 7). This study examines allogeneic stem cell transplantation in the treatment of AML and changes in outcomes over time.

The number of patients registered with the diagnosis C92 (myeloid leukaemia) – excluding C92.1 (chronic myeloid leukaemia, *BCR::ABL1*-positive) and C92.2 (atypical chronic myeloid leukaemia, *BCR::ABL1*-negative) – C93.0 (acute monoblastic/monocytic leukaemia), C94.0 (acute erythroid leukaemia) and C94.2 (acute megakaryoblastic leukaemia) in the various regional health authorities was obtained from the Cancer Registry of Norway for the same time period (8). The data from the Cancer Registry databases are 94.9 % complete for malignant blood disorders (ICD codes C91–95) (9).

Statistical analyses

Descriptive statistics were used, reporting the median, range and percentages. Survival was defined as the time from transplantation to death or censoring. Survival and transplant-related mortality were estimated using Kaplan-Meier plots and log-rank tests. Results are presented in five-year intervals. In the survival analyses, patients who experienced relapse and were subsequently retransplanted were excluded. Analyses were performed using Statistica version 13.5 (TIBCO, Palo Alto, CA, USA) and EZR version 1.61 (Saitama Medical Center, Jichi Medical University, Saitama, Japan). Differences where $p < 0.05$ were considered statistically significant.

Ethics

The Norwegian Directorate of Health requires the multi-regional treatment service for allogeneic stem cell transplantation to maintain a registry tracking activity and quality. The Transplant Registry has been approved by the data protection officer and by the Regional Committee for Medical and Health Research Ethics (REK) for publication (REK South-East 11909/2021).

Results

In the period 1 January 2005 to 31 December 2022, a total of 2979 people were diagnosed with AML. The distribution across the four regional health authorities, as well as the patients' median age and age range, is presented in Table 1. The median age at diagnosis was 70 or 71 years in the different regional health authorities.

Out of 2979 patients with AML, 674 (22.6 %) underwent allogeneic stem cell transplantation. Eighty-eight patients were transplanted at Haukeland University Hospital and 586 at Oslo University Hospital. Detailed characteristics of these transplanted patients are shown in Table 2. The median age at diagnosis was 70–71 years, and very few patients above this age were transplanted. This indicates that just under 45 % of those younger than 70–71 years received a transplant. The number of patients with AML who underwent allogeneic stem cell transplantation gradually increased over the study period, from 14 in 2005 to a peak of 67 in 2020 (Figure 1).

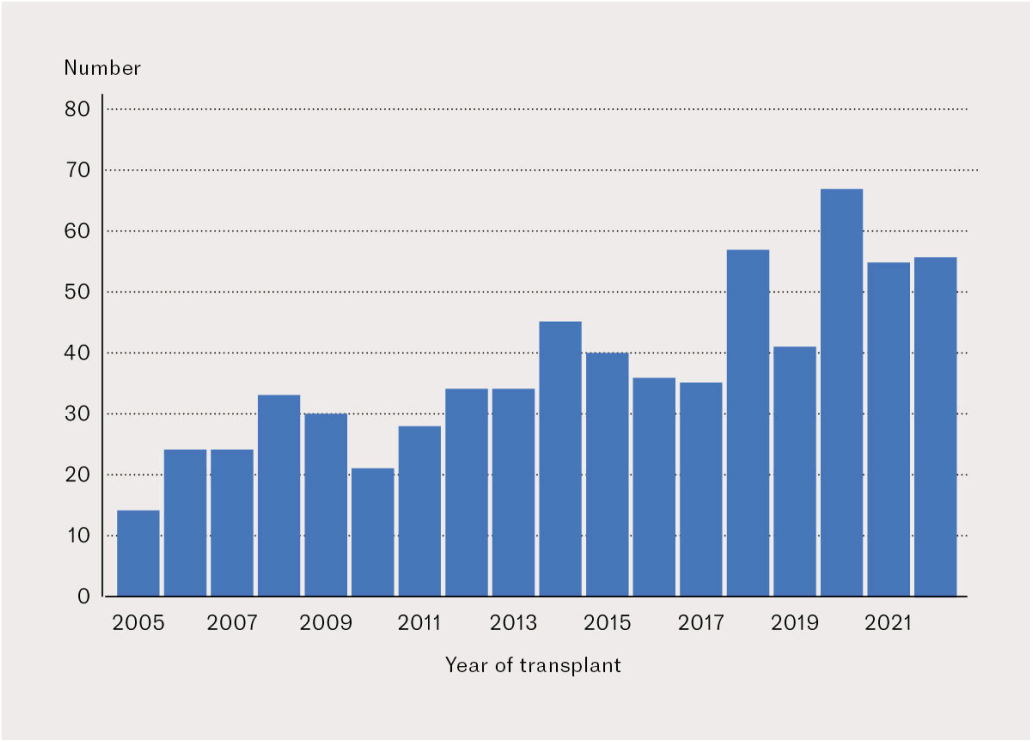


Figure 1 The figure shows the annual number of allogeneic stem cell transplants performed in Norway for AML during the period 1 January 2005–31 December 2022. In 2005, stem cell transplants were only performed at Oslo University Hospital.

Five-year survival was 48 % for patients transplanted in the period 2005–10, 53 % in 2011–16 and 63 % in 2017–22 (Figure 2). The difference in survival between the first and last periods is statistically significant ($p = 0.006$). Improved survival coincided with a reduction in treatment-related mortality (Figure 3), and the difference in treatment-related mortality between the first and last periods is statistically significant ($p < 0.001$).

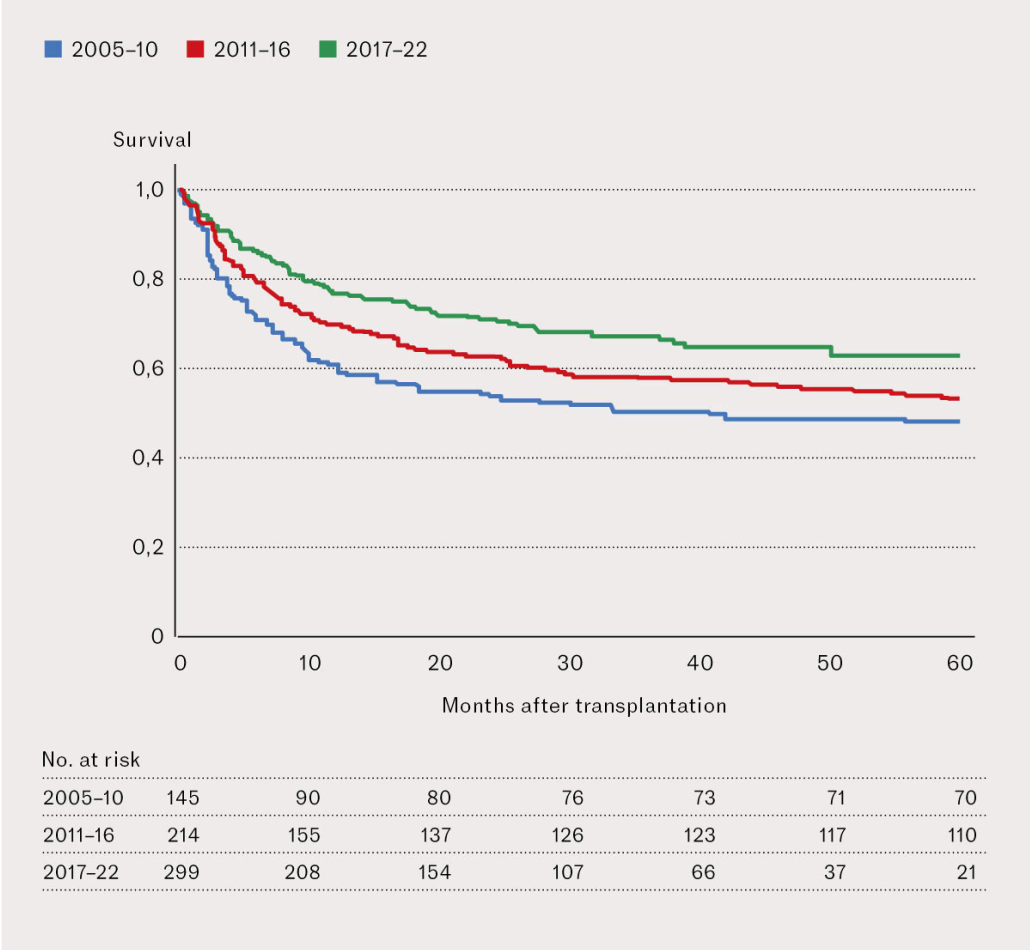


Figure 2 The Kaplan-Meier curves show survival after allogeneic stem cell transplantation for AML during the periods 2005–10 (blue curve), 2011–16 (red curve) and 2017–22 (green curve). The improved survival in the period 2017–22 compared to 2005–10 is statistically significant (p = 0.006). Patients who relapsed and were subsequently retransplanted are not included in the survival analyses.

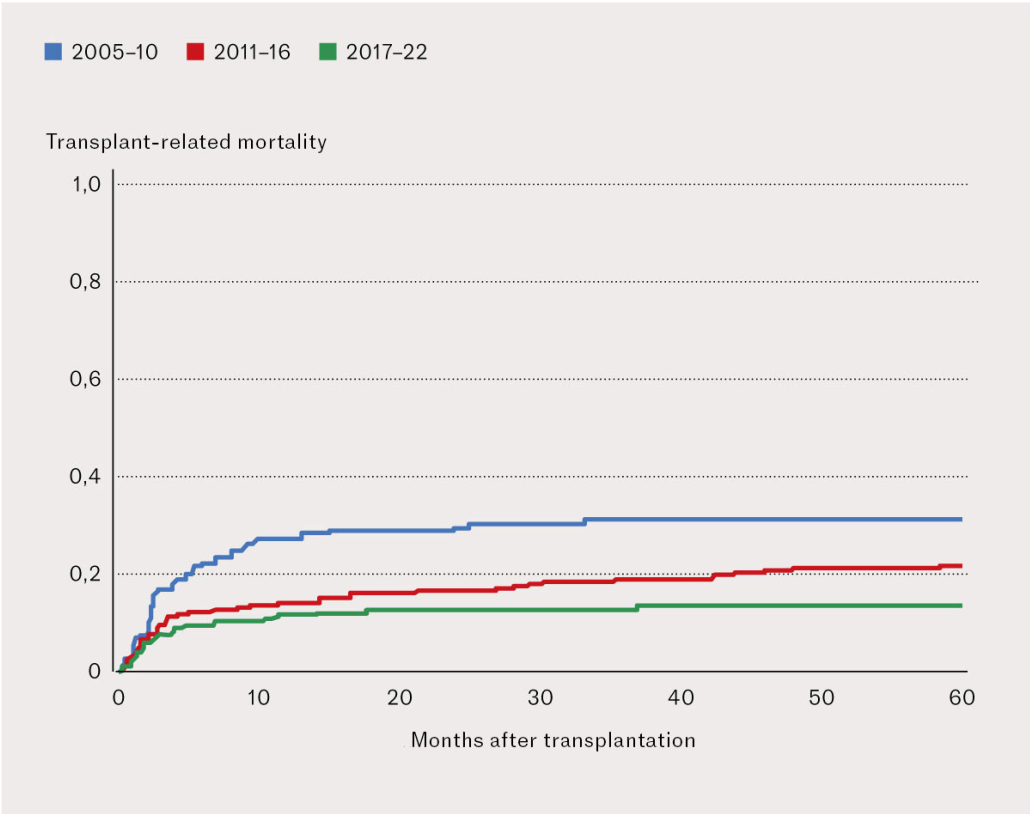
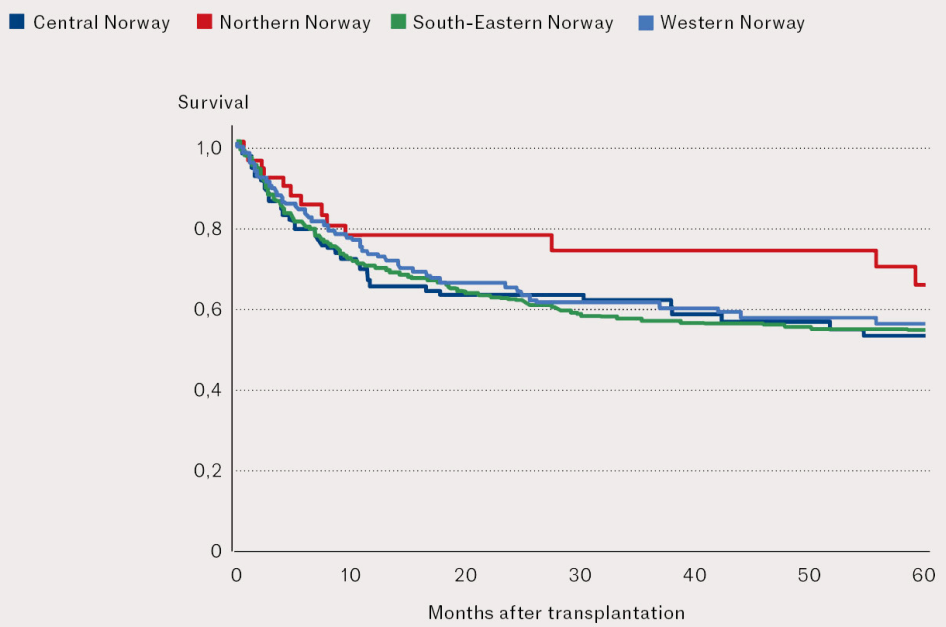


Figure 3 The curves show transplant-related mortality during the periods 2005–10 (blue curve), 2011–16 (red curve) and 2017–22 (green curve). The difference in transplant-related mortality between the periods 2005–10 and 2017–22 is statistically significant ($p < 0.001$). The number at risk is identical to that inFigure 2.

A similar proportion of patients with AML underwent allogeneic stem cell transplantation across the four regional health authorities: 403 of 1734 patients (23.2 %) from South-Eastern Norway, 134 of 585 patients (22.9 %) from Western Norway, 88 of 404 patients (21.7 %) from Central Norway and 49 of 256 patients (18.3 %) from Northern Norway. There was no statistically significant difference between the regions regarding gender ($p = 0.15$). No statistically significant difference in survival was observed between the regional health authorities, even though transplanted patients from Western and Central Norway had a lower median age than those from Northern and South-Eastern Norway (Figure 4 and Table 2). A total of 455 out of 674 (67.5 %) patients were transplanted in first complete haematologic remission, with only a slight regional variation (Table 2).



Number at risk							
Central Norway	87	60	51	48	35	31	28
Northern Norway	48	32	29	23	22	19	15
South-Eastern Norway	392	264	218	179	155	134	123
Western Norway	131	97	73	59	50	41	35

Figure 4 The Kaplan-Meier curves show survival after allogeneic stem cell transplantation for AML in patients from the four regional health authorities during the period 1 January 2005–31 December 2022. Northern Norway (red curve), Central Norway (dark blue curve), Western Norway (light blue curve) and South-Eastern Norway (green curve). The seemingly better survival for patients from Northern Norway is not statistically significant: p = 0.065.

Discussion

Allogeneic stem cell transplantation was performed in 674 (22.6 %) of the 2979 patients diagnosed with AML during the study period, with the number of procedures increasing steadily over time. The annual number of transplants more than doubled from the period 2005–10 to 2017–22. Alongside the increased use of stem cell transplantation in AML, treatment outcomes improved: five-year survival rose from 48 % in the first period to 63 % in the second.

Our data confirm that allogeneic stem cell transplantation is now a central component of treatment for AML in Norway. AML is the most common indication for allogeneic stem cell transplantation in Norway, as well as in Europe and North America (4, 5, 10). In Norway, it is primarily used as part of first-line treatment, as in the rest of Europe (5). A study published in 2023 showed that 18 % of all patients with AML, and 36 % of patients under 70 years of age, underwent allogeneic stem cell transplantation in Europe in 2016 (10). Although this is a slightly lower proportion than observed in Norway, the difference is likely attributable to our data also encompassing the period 2017–22. The number of transplants increased both in Norway (Figure 1) and in Europe during this period (5, 10). No differences were found between the various regional health authorities in the use of allogeneic stem cell transplantation for AML.

Not all patients with AML should be offered allogeneic stem cell transplantation. In patients with low-risk disease, defined by specific cytogenetic abnormalities in the leukaemia cells, chemotherapy alone yields such favourable outcomes that transplantation is only indicated for the small subset of patients who relapse after chemotherapy. This applies to approximately 15 % of AML patients (2). Others are not eligible for allogeneic stem cell transplantation because they have chemotherapy-resistant disease (10–20 %) (2, 9), while some have such severe comorbidities that transplantation is not advisable due to the very high risk of transplant-related mortality (3).

There is no upper age limit for allogeneic stem cell transplantation in Norway or the rest of Europe. However, age is a risk factor for transplant-related mortality, and the likelihood of comorbidities also increases with age (3, 8). No substantial differences were found in patient age between the regional health authorities among those who underwent allogeneic stem cell transplantation for AML. The age range was similar across regions, although the median age of patients from Central and Western Norway was slightly lower than for Northern and South-Eastern Norway. New conditioning regimens better tailored to individual patients and their illness have been developed throughout the study period. This has made it possible to offer allogeneic stem cell transplantation to more patients than before, while transplant-related mortality has been reduced (4). As a result, increasingly older patients have become eligible for this treatment. The median age has risen from 28 years in

the period 1985–90 to nearly 60 years today (4, 7). Antithymocyte globulin (ATG) was routinely used from 2014 to prevent graft-versus-host disease. Donor-derived T-lymphocytes are crucial for the development of graft-versus-host disease but they also play a key role in the graft-versus-leukaemia effect (12). ATG induces a dose-dependent reduction in T-lymphocytes, and to maintain a strong antileukemic effect while preventing graft-versus-host disease, a balanced reduction of donor T-lymphocytes is necessary. The introduction of ATG has substantially reduced transplant-related mortality (4, 11, 12).

The National Group for Allogeneic Stem Cell Transplantation was established in the early 1990s, with all regional health authorities represented by one or more haematologists. The group has developed and continuously revised the indications for allogeneic stem cell transplantation. The treatment is a well-established option for AML, and since 2012, treatment centres in Norway have followed national guidelines for AML and other malignant blood disorders (13). The indications for allogeneic stem cell transplantation have been incorporated into these guidelines. This has likely been a key factor in supporting the standardised and increasing use of allogeneic stem cell transplantation to treat AML.

Conclusion

In Norway, allogeneic stem cell transplantation is increasingly being used as a central component in the treatment of AML, as in the rest of Europe. Treatment outcomes continue to improve, primarily due to a reduction in transplant-related mortality. No evidence was found of unequal access to the multi-regional treatment service.

The article has been peer-reviewed.

REFERENCES

1. Cancer Registry of Norway. Cancer in Norway 2022 – Cancer incidence, mortality, survival and prevalence in Norway. Oslo: Cancer Registry of Norway, 2023. https://www.fhi.no/globalassets/cancer-in-norway/2022/cin_report-2022.pdf Accessed 31.7.2025.

2. Tangen JM, Fløisand Y, Foss-Abrahamsen J et al. Overlevelse hos voksne med akutt myelogen leukemi. Tidsskr Nor Lægeforen 2008; 128: 1164–7. [PubMed]

3. Loke J, Buka R, Craddock C. Allogeneic stem cell transplantation for acute myeloid leukemia: Who, When and How. Front Immunol 2021; 12. doi: 10.3389/fimmu.2021.659595. [PubMed][CrossRef]

4. Vo CD, Myhre AE, Abrahamsen IW et al. Allogen stamcelletransplantasjon hos voksen 2015-2021. Tidsskr Nor Legeforen 2023; 143: 322–8.

5. Tokaz MC, Baldomero H, Cowan AJ et al. An Analysis of the Worldwide Utilization of Hematopoietic Stem Cell Transplantation for Acute Myeloid Leukemia. Transplant Cell Ther 2023; 29: 279.e1–10. [PubMed][CrossRef]

6. Helse- og omsorgsdepartementet. Forskrift om krav til spesialisthelsetjenester, godkjenning av nasjonale tjenester i spesialisthelsetjenesten og bruk av betegnelsen universitetssykehus – Kapittel 4. Godkjenning av nasjonale tjenester i spesialisthelsetjenesten. https://lovdata.no/dokument/SF/forskrift/2010-12-17-1706/KAPITTEL_4#KAPITTEL_4 Accessed 12.6.2024.

7. Husøy MAR, Brinch L, Tjønnfjord GE et al. Allogen stamcelletransplantasjon hos voksne 1985-2012. Tidsskr Nor Legeforen 2014; 134: 1569–75. [PubMed]

8. Nordcan. Absolute numbers, Incidence, Both sexes. Acute myeloid leukaemias. https://nordcan.iarc.fr/en/dataviz/trends?cancers=404&years_available=1943_2023&sexes=0&populations=578&key=total&mode=population&multiple_populations=1 Accessed 1.6.2024.

9. Larsen IK, Småstuen M, Johannesen TB et al. Data quality at the Cancer Registry of Norway: an overview of comparability, completeness, validity and timeliness. Eur J Cancer 2009; 45: 1218–31. [PubMed][CrossRef]

10. Passweg JR, Baldomero H, Ciceri F et al. Hematopoietic cell transplantation and cellular therapies in Europe 2022. CAR-T activity continues to grow; transplant activity has slowed: a report from the EBMT. Bone Marrow Transplant 2024; 59: 803–12. [PubMed][CrossRef]

11. Baron F, Mohty M, Blaise D et al. Anti-thymocyte globulin as graft-versus-host disease prevention in the setting of allogeneic peripheral blood stem cell transplantation: a review from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. Haematologica 2017; 102: 224–34. [PubMed][CrossRef]

12. Ali MM, Grønvold B, Remberger M et al. Addition of anti-thymocyte globulin in allogeneic stem cell transplantation with peripheral stem cells from matched unrelated donors improves graft-versus-host disease and relapse free survival. Clin Lymphoma Myeloma Leuk 2021; 21: 598–605. [PubMed][CrossRef]

13. Helsedirektoratet. Nasjonalt handlingsprogram med retningslinjer for diagnostikk, behandling og oppfølging av maligne blodsykdommer. https://www.helsedirektoratet.no/retningslinjer/maligne-blodsykdommer--handlingsprogram Accessed 12.6.2024.

Publisert: 8 October 2025. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.25.0001
Received 2.1.2025, first revision submitted 10.3.2025, accepted 31.7.2025.