GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

# Specialised Services Policy Position PP142

## Haematopoietic Stem Cell Transplantation (HSCT) for Adults

*January 2020*

*Version 1.0*

| Document information | |
|---|---|
| **Document purpose** | Policy Position |
| **Document name** | Haematopoietic Stem Cell Transplantation (HSCT) for adults |
| **Author** | Welsh Health Specialised Services Committee |
| **Publication date** | October 2019 |
| **Revision Date** | November 2022 |
| **Commissioning Team** | Cancer and Blood |
| **Target audience** | Chief Executives, Medical Directors, Directors of Finance, Chief Pharmacists, Haematology Clinical Leads |
| **Description** | NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy |
| **Document No** | PP142 |
| **Review Date** | February 2025 |

# Contents

# Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission Haematopoietic Stem Cell Transplantation (HSCT) for adults resident in Wales in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed the relevant guidance issued by NHS England and has concluded that blood and marrow transplantation should be made available.

## Disclaimer

WHSSC assumes that healthcare professionals will use their clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply this policy position statement.

This policy may not be clinically appropriate for use in all situations and does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

WHSSC disclaims any responsibility for damages arising out of the use or non-use of this policy position statement.

# 1. Introduction

This Policy Position has been developed for the planning and delivery of Haematopoietic Stem Cell Transplantation (HSCT) for adults resident in Wales. This service will only be commissioned by the Welsh Health Specialised Services Committee (WHSSC) and applies to residents of all seven Health Boards in Wales.

Stem cell transplantation, particularly allogeneic transplantation, is a high cost and highly specialised procedure, performed by skilled and experienced transplant teams working in specialist centres. Allogeneic transplantation carries relatively high mortality and morbidity risks, and these must be weighed against the potential longer-term survival benefits when considering a patient for transplantation. Rigorous patient selection is of paramount importance.

Because of the large number of possible indications for stem cell transplantation, the degree of variation in clinically important patient and disease parameters, and the diversity of conditioning and transplant regimens, it is extremely difficult to evaluate the clinical and cost-effectiveness of transplantation for every potential clinical condition. Moreover, age is an important factor in determining outcomes; thus the management of children and young people is very different to that in older adults. For all these reasons, current clinical practice in stem cell transplantation is largely based on clinical consensus and published case series.

This policy document sets out the clinical indications for which autologous and allogeneic transplants will be commissioned routinely by NHS Wales for adults.

For a more detailed description of the transplantation services which will be commissioned and the service standards which should be met by transplant centres please refer to the WHSSC Service Specification for Haematopoietic Stem Cell Transplant (CP79)

## 1.1 Plain language summary

Haematopoietic Stem Cell Transplantation (HSCT) is also known as blood and marrow transplantation (BMT). It is used to treat a wide spectrum of disorders. It is broadly divided into two main groups: autologous and allogeneic transplantation.

Allogeneic haematopoietic stem cell transplantation (HSCT) is used to treat carefully selected patients with a range of malignant and non-malignant blood-related disorders and other specific disorders of the immune system. It involves replacing the bone marrow stem cells of a patient following high-

dose therapy, with stem cells from a tissue-type matched or mismatched donor.

Autologous transplantation uses the patient's own stem cells, which are harvested prior to high-dose therapy. It enables the patient to be treated with doses of chemotherapy which are higher than would be possible without subsequent replacement of the harvested cells, because the therapy destroys the patient's remaining stem cell tissue.

## 1.2 Aims and Objectives

This Policy Position aims to define the commissioning position of WHSSC on the use of Haematopoietic Stem Cell Transplantation (HSCT) for adults.

The objectives of this policy are to:

- ensure commissioning for the use of HSCT is evidence based
- ensure equitable access to HSCT
- define criteria for people to access treatment
- improve outcomes for people with undergoing HSCT

## 1.3 Epidemiology

The data below are taken from the British Society of Blood and Marrow Transplantation (BSBMT)[1] registry for stem cell transplant procedures undertaken by HSCT centres in the UK and Republic of Ireland. The figures include repeat transplants (including donor lymphocyte infusions) in patients who have previously been transplanted. There are considerable year to year fluctuations in numbers, but an underlying increasing trend.

**Table 1: Number of transplants by transplant type 2006-2016 inclusive**

| Year | Allo | Autografts | Total | % Increase |
|---|---|---|---|---|
| 2006 | 1144 | 1562 | 2706 | 0 |
| 2007 | 1198 | 1569 | 2767 | 2.2 |
| 2008 | 1263 | 1676 | 2939 | 5.8 |
| 2009 | 1200 | 1623 | 2823 | -4.11 |
| 2010 | 1321 | 1919 | 3240 | 12.9 |
| 2011 | 1443 | 1917 | 3360 | 3.6 |
| 2012 | 1453 | 2163 | 3616 | 7 |
| 2013 | 1615 | 2225 | 3840 | 5.8 |
| 2014 | 1678 | 2344 | 4022 | 4.5 |
| 2015 | 1610 | 2503 | 4113 | 2.2 |
| 2016 | 1680 | 2718 | 4398 | 6.9 |

[1] http://bsbmt.org/activity/2016/

Table 2 below shows a breakdown of first transplants by clinical indication for 2016. Myelomas and lymphomas remain the most common indications for autologous transplantation. Most allogeneic transplants are for acute leukaemias, followed by the lymphomas.

**Table 2: Number of first transplants by disease category and transplant type 2016**

| Indication | Allograft | Autograft | Total |
|---|---|---|---|
| Plasma Cell Disease | 43 | 1467 | 1510 |
| Lymphoma | 206 | 756 | 962 |
| Acute Leukaemia | 801 | 9 | 810 |
| MDS/MPS | 261 | 0 | 261 |
| Solid Tumour | 0 | 143 | 143 |
| Chronic Leukaemia | 78 | 2 | 80 |
| Primary Immune Deficiency | 59 | 0 | 59 |
| Bone Marrow Failure | 87 | 4 | 91 |
| Haemoglobinopathy | 29 | 0 | 29 |
| Inherited Disorders of Metabolism | 17 | 0 | 17 |
| Auto Immune Diseases | 8 | 41 | 49 |
| Other | 14 | 2 | 16 |
| Total | 1603 | 2474 | 4027 |

## 1.4 About the treatment

Allogeneic haematopoietic stem cell transplantation (HSCT) is used to treat carefully selected patients with a range of malignant and non-malignant haematological disorders and other specific disorders of the immune system. It involves replacing the bone marrow stem cells of a patient following high-dose therapy, with stem cells from a tissue-type matched or mismatched donor.

Patients require detailed pre-transplant assessment and investigations to assess their clinical status and fitness to proceed to transplant. The transplant procedure begins with 'conditioning' therapy (chemotherapy with or without total body irradiation (TBI)) at a range of doses depending on the type and severity of disease being treated. The aim of conditioning is to:

- kill leukaemia/tumour cells (in malignant diseases)
- suppress the patient's immune system, so as to minimise the risk of graft rejection

Bone marrow, peripheral blood stem cells, or umbilical cord blood stem cells may be used as donor stem cell sources. Use of umbilical cord cells must be in line with the UK Cord Blood Working Group Recommendations for donor selection[2]. Use of double cord units must be notified in advance to

[2] https://www.transfusionguidelines.org/dsg/cb

the commissioner in view of the likely increased costs and to ensure the selection protocol has been followed.

Autologous transplantation uses the patient's own stem cells, which are harvested prior to high-dose therapy. It is performed as part of dose escalation therapy, mainly in patients with lymphoma and myeloma, although it is also used in certain autoimmune and oncology cases. It enables the patient to be treated with doses of chemotherapy which are higher than would be possible without subsequent replacement of the harvested cells, because the therapy destroys the patient’s remaining stem cell tissue.

## 1.5 What NHS Wales has decided

WHSSC has carefully reviewed the relevant guidance issued by NHS England. We have concluded that there is enough evidence to fund HSCT within the criteria set out in section 2.1.

# 2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of Haematopoietic Stem Cell Transplantation (HSCT) for adults in-line with the criteria identified in the policy.

## 2.1 Inclusion Criteria

Adult Haematopoietic Stem Cell Transplantation (HSCT) is commissioned according to the British Society of Blood and Marrow Transplantation (BSBMT) table of indications published in February 2012 as specified in Appendix 1.

BSBMT recommendations divide indications for adult Haematopoietic Stem Cell Transplantation (HSCT) into four categories:

| Category | Abbreviation |
|---|---|
| Standard of care | S |
| Clinical option, can be considered after assessment of risks and benefits | CO |
| Developmental, further trials are needed | D |
| Generally not recommended | GNR |

For the purposes of this commissioning policy first transplants for indications within categories S and CO (standard of care, and clinical option respectively) are accepted as established clinical practice, and will be commissioned routinely, without the need for Individual Funding Request (IPFR).

Repeat transplants for failure to engraft will also be commissioned routinely. However, repeat autologous or allogeneic transplants for relapsed disease will not be commissioned routinely unless explicitly recommended by the BSBMT guidelines (e.g. second autologous transplant for myeloma and POEMS).

Use of umbilical cord cells must be in line with the UK Cord Working Group Recommendations for donor selection[3]. Use of double cord must be notified in advance to the commissioner to demonstrate the donor selection protocol has been followed.

Patients can be entered into clinical trials by the provider where the patient's treatment will comply with this Policy Position. Where the treatment falls outside the Policy, prior approval must be sought from WHSSC before entering the patient into the trial.

[3] https://www.transfusionguidelines.org/dsg/cb

WHSSC will not pay for treatment for indications which are outside this Policy Position and for which prior approval has not been formally given.

## 2.2 Exclusion Criteria

Areas excluded from this commissioning policy are:

- Second allogeneic transplants for relapse disease will not be routinely commissioned for patients who have relapsed after first Allo-HSCT.
- Repeat autologous or allogeneic transplants for relapsed disease unless explicitly recommended by the BSBMT guidelines (e.g. second autologous transplant for myeloma and POEMS). IPFR approval will otherwise need to be sought.
- Planned tandem transplants unless explicitly recommended by the BSBMT guidelines. IPFR approval will otherwise need to be sought.
- Transplants for indications within categories D and GNR will not be commissioned routinely, and IPFR approval will need to be sought for transplantation of all cases falling within these categories where cases meet the criteria for exceptionality.
- Haematopoietic Stem Cell Transplantation (HSCT) is not commissioned for any indication which is not listed within the BSBMT (February 2012) table of indications for indications listed in BSBMT indications tables published after February 2012 unless they are specifically confirmed in this policy. IPFR approval will therefore need to be sought for transplantation for all indications not specifically listed in the appendix of this policy document.
- Children under the age of 18

## 2.3 Acceptance Criteria

The service outlined in this specification is for patients ordinarily resident in Wales, or otherwise the commissioning responsibility of the NHS in Wales. This excludes patients who whilst resident in Wales, are registered with a GP practice in England, but includes patients resident in England who are registered with a GP Practice in Wales.

## 2.4 Patient Pathway (Annex i)

Referral is from secondary care consultant clinicians including haematologists, oncologists and, rarely, from other non-cancer specialists such as neurologists, immunologists and rheumatologists.

All patients with haematological malignancies should be discussed at, and referred by, their local Haematology Cancer MDT.

Referrals should be made to the Haematopoietic Stem Cell Transplantation (HSCT) centre.

A clearly defined aftercare programme shall be developed with the patient and the referring provider unit. Communication with general practitioners and staff in primary care and the referring clinician shall be timely, efficient and continuous. The GP shall be informed at all stages of the patient's treatment. Patients will be informed how to access advice and urgent care at all stages of their treatment.

Unless the urgent need for treatment precludes the possibility, all patients of reproductive age shall be offered a review by reproductive medicine prior to starting infertility-inducing treatment.

## 2.5 Exceptions

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If the patient wishes to be referred to a provider outside of the agreed pathway, and IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

## 2.6 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to the lead commissioner.

The centre must enable the patient's, carer's and advocate's informed participation and to be able to demonstrate this. Provision should be made for patients with communication difficulties.

All providers of HSCT must have JACIE accreditation.

## 2.7 Audit Requirements

Complete data must be submitted to the BSBMT registry for all transplants carried out by UK centres.

All centres must undergo regular JACIE inspection.

All centres must provide the data required for the English national BMT Dashboard

Audit requirements are described in more detail in the WHSSC Service Specification for Haematopoetic Stem Cell Transplantation (CP79).

## 2.8 Responsibilities

Referrers should:

- inform the patient that this treatment is not routinely funded outside the criteria in this policy, and
- refer via the agreed pathway.

Clinicians considering treatment should:

- discuss all the alternative treatment with the patient
- advise the patient of any side effects and risks of the potential treatment
- inform the patient that treatment is not routinely funded outside of the criteria in the policy, and
- confirm that there is contractual agreement with WHSSC for the treatment.

In all other circumstances an IPFR must be submitted.

## 3. Documents which have informed this policy

This WHSSC policy position adopts the commissioning criteria of the NHS England commissioning policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised. NHS England B04/P/a January 2015.

This document should be read in conjunction with the following documents:

- **NHS Wales**
  - All Wales Policy: Making Decisions in Individual Patient Funding requests (IPFR).

- **WHSSC policies and service specifications**
  - Haematopoietic Stem Cell Transplantation for Adults (CP79), Service Specification, (Publication Date to be confirmed)
  - Extra corporeal Photophoresis (ECP) for the Treatment of Chronic Graft versus Host Disease in Adults (CP91). WHSSC, Specialised Services Commissioning Policy, November 2015.
  - Extracorporeal Photophoresis (ECP) for the Treatment of Cutaneous T-cell Lymphoma (CP92). WHSSC Specialised Services Commissioning Policy. November 2015.

- **National Institute of Health and Care Excellence (NICE) guidance**
  - Haematological Cancers: Improving Outcomes. NICE Guideline NG47, May 2016.

- **Relevant NHS England policies**
  - Haematopoietic Stem Cell Transplantation (HSCT) All Ages, Revised. Clinical Commissioning Policy, NHS England B04/P/a. January 2015.
  - 2013/2014 NHS Standard Contract for Haematopoietic Stem Cell Transplantation (Adult). NHS England Service Specification, B04/S/a. October 2013.

- **British Society for Blood and Marrow Transplants (BSBMT)**
  - British Society for Blood and Marrow Transplants. BSBMT Indications for Adult BMT

## 4. Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

# 5. Putting Things Right

## 5.1 Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided.

The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern.

If a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for NHS Putting Things Right. For services provided outside NHS Wales the patient or their representative should be guided to the NHS Trust Concerns Procedure, with a copy of the concern being sent to WHSSC.

## 5.2 Individual Patient Funding Request (IPFR)

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent review of the process to be undertaken by the patient's Local Health Board. The ground for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated

If the patient wishes to be referred to a provider outside of the agreed pathway, an IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

# 6. Equality Impact and Assessment

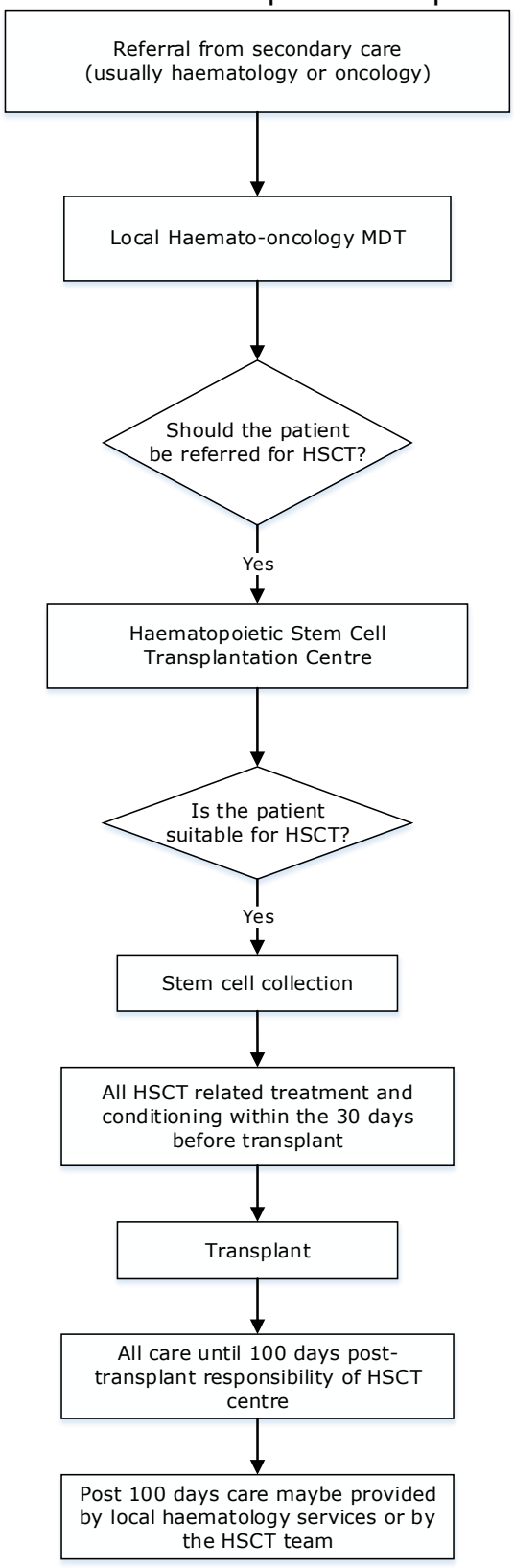
The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (Welsh).

This policy has been subjected to an Equality Impact Assessment.

The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

# Annex i Patient Pathway

Adult Haematopoietic Stem Cell Transplantation pathway



# Annex ii Checklist

## Blood and Marrow Transplantation

The following checklist should be completed for every patient to whom the policy applies:

- Where the patient meets the criteria **and** the procedure is included in the contract **and** the referral is received by an agreed centre, the form should be completed and retained by the receiving centre for audit purposes.
- The patient meets the criteria **and** is received at an agreed centre, but the procedure is not included in the contract. The checklist must be completed and submitted to WHSSC for prior approval to treatment.
- The patient meets the criteria but wishes to be referred to a non-contracted provider. An Individual Patient Funding Request (IPFR) Form must be completed and submitted to WHSSC for consideration.
- If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

# Annex iii Codes

| Code Category | Code | Description |
|---|---|---|
| OPCS | W341 | Autograft of bone marrow |
| | W342 | Allograft of bone marrow NEC |
| | W343 | Allograft of bone marrow from sibling donor |
| | W344 | Allograft of bone marrow from matched unrelated donor |
| | W345 | Allograft of bone marrow from haploidentical donor |
| | W346 | Allograft of bone marrow from unmatched unrelated donor |
| | W348 | Other specified graft of bone marrow |
| | W349 | Unspecified graft of bone marrow |
| | W991 | Allograft of cord blood stem cells to bone marrow |
| | W998 | Other specified graft of cord blood stem cells to bone marrow |
| | W999 | Unspecified graft of cord blood stem cells to bone marrow |

# Annex iv Abbreviations and Glossary

## Abbreviations

**IPFR** Individual Patient Funding Request

**WHSSC** Welsh Health Specialised Services Committee

## Glossary

### Individual Patient Funding Request (IPFR)

An IPFR is a request to Welsh Health Specialised Services Committee (WHSSC) to fund an intervention, device or treatment for patients that fall outside the range of services and treatments routinely provided across Wales.

### Welsh Health Specialised Services Committee (WHSSC)

WHSSC is a joint committee of the seven local health boards in Wales. The purpose of WHSSC is to ensure that the population of Wales has fair and equitable access to the full range of Specialised Services and Tertiary Services. WHSSC ensures that specialised services are commissioned from providers that have the appropriate experience and expertise. They ensure that these providers are able to provide a robust, high quality and sustainable services, which are safe for patients and are cost effective for NHS Wales.

# Appendix 1 BSBMT Indications for BMT – February 2012

## Abbreviations:

| | |
|---|---|
| S | Standard of Care |
| CO | Clinical option, can be considered after assessment of risks and benefits |
| D | Developmental, further trials are needed |
| GNR | Generally Not Recommended |

# Section 1

## CML

| | Sibling Allograft | Unrelated donor transplant | Autologous transplant |
|---|---|---|---|
| **Chronic phase**<br>TKI refractory[1] (after trial of at least 2 TKIs) | S[1,2,3] | S[1,2,3] | GNR |
| TKI intolerant (Grade 2+ toxicity to at least 2 TKIs) | S[1] | S[1] | GNR |
| T315I mutation | S[1] | S[1] | GNR |
| **Accelerated phase**<br>-after initial therapy with TKI | S[4,5] | S[4,5] | GNR |
| **Blast crisis** | GNR | GNR | GNR |
| **2nd chronic phase** | S[4,6] | S[4,6] | D[7] (if Ph –ve cells have been stored) |

[1]For definition see Baccarani et al


[1]Baccarani et al, 2009, J Clin Onc 27: 6041-6051
[2] Lee et al, Blood 2008, 112: 3500-3507
3 Bacher et al, Ann Haematol 2009, 88: 1237-1247
[4] Saussale et al, Blood 2010 115: 1880-1885
[5] Jiang et al, Blood 2011, 117: 3032-40
[6] Weisser et al, Leuk Lymphoma 2007, 48: 295-301
[7]Bhatia et al, Haem/Onc Clin North Am 2004, 18 : 715-732

***Myeloma***

| | **Sibling transplant‡** | **MUD transplant** | **First Autograft** | **Second Autograft** |
|---|---|---|---|---|
| First Line | S[16, 17] | CO[18]<br>-Selected patients or as part of clinical trial | S[9]<br>-for patients suitable for intensive treatment | CO[10,11]<br>(Tandem autograft may be considered if no CR after 1st autograft) |
| Relapse | CO[12, 19] | CO<br>-Selected patients or as part of clinical trial | S<br>(If not done in first response but patient is considered fit) | S[13]<br>-If time to re-treatment after 1st autograft >18m or as part of NCRN Myeloma X trial |
| Plasma cell leukaemia | S[15]<br>-If chemo responsive disease<br>-Selected young patients <55 years | CO[15]<br>-If chemo responsive disease | S[15]<br>-If no suitable donor or unfit for allograft | CO |

‡ *- Suitability for a myeloablative versus reduced-intensity is based on biological suitability (age, co morbidity, advanced disease stage, etc)*

References:


8. Gahrton et al, Haematologica 2007, 92: 1513-8
9. Child et al, New Engl J Med 2003, 348: 1875-8
10. Abdellcefi et al, Blood 2007, e-pun Nov 8
320-32 11. Cavo et a, J Clin Onc 2007, 25: 2434-41
12. Elice et al, Am J Haematol 2006, 81: 426-31
13. Alvares et al, Haematologica 2006, 91: 141-2
14. Perfetti et al, Haematologica 2006, 91: 1635-43
15. Saccaro et al, Am J Haematol, 2005, 78: 288-94
16. Levenga H et al, Biol Blood Marrow Transplant, 2010 Mar: 16(3):
17. Rotta et al, Blood, 2009 Apr 2: 113 (14): 3383-91
18. Kroeger et al, Br J Haematol, 2010 Jan; 148(2): 323-31
19. Efebera YA et al, Biol Blood Marrow Transplant, 2010 Feb 20

***Other Plasma Cell Dyscrasias***

| | Sibling transplant | MUD transplant | First Autograft | Second Autograft |
|---|---|---|---|---|
| **AL amyloid** | GNR | GNR | CO[14] -As per risk-adapted protocol | GNR |
| **POEMS** | GNR | GNR | CO[16] | CO[13] -If time to re-treatment after 1st autograft >18m or as part of a clinical study |

References:

13. Jaccard et al, Blood 2002, 99: 3055-9
14. Perfetti et al, Haematologica 2006, 91: 1635-43

General Comments

1. Generally RIC transplants are performed for patients >45-50 years of age or for patients with significant co-morbidities using the HSCT co-morbidity index. In the context of certain clinical trials the age for choosing a RIC transplant may be lower. Patients with a score >3 are generally not suitable for any HSCT
2. For unrelated donor transplants usually either a full 10/10 match at HLA A, B, C and DR is required or a single mismatch
3. Cord Blood transplants are an alternative for patients lacking a sibling or unrelated donor (as defined above). Usually these patients are from ethnic minority.

## Section 2

### *AML*

| | | Sibling transplant | MUD transplant | Autograft | Comments |
|---|---|---|---|---|---|
| **APL CR1**<br>**APL CR2**<br>**PCR+**<br>**APL CR2 PCR-** | | GNR<br>S<br><br>CO | GNR<br>S<br><br>GNR | GNR<br>GNR<br><br>S | BCSH guidelines |
| **AML -good risk** | **CR1**<br>**CR2** | GNR<br>S | GNR<br>S | GNR<br>CO | BCSH guidelines<br>AML15/16 trial protocols |
| **AML -standard risk** | **CR1** | S | S | GNR | AML 15/16 protocols |
| | **CR2** | S | S | CO | |
| **AML -poor risk*** | **CR1**<br>**CR2** | S | S | GNR | AML 15/16 protocols |
| | | S | S | CO | |
| **AML not in remission** | | CO | CO | GNR | Fung et al[1], Cook et al[2] |

* Poor risk defined as either 1. cytogenetics (MRC criteria), 2. Secondary or therapy – related AML, 3. Failure to achieve CR with standard AML induction therapy

References

1. Fung HC, Stein A, Slovak M, et al. A long-term follow-up report on allogeneic stem cell transplantation for patients with primary refractory acute myelogenous leukemia: impact of cytogenetic characteristics on transplantation outcome. Biol Blood Marrow Transplant. 2003;9:766771
2. Cook G, Clark RE, Crawley C, et al. The outcome of sibling and unrelated donor allogeneic stem cell transplantation in adult patients with acute myeloid leukemia in first remission that were initially refractory to first induction chemotherapy. Biol Blood Marrow Transplant. 2006;12:293-300

## Section 3

### *ALL*

| | Sibling transplant | MUD transplant | Autograft |
|---|---|---|---|
| **CR1**<br>**-standard risk**<br>**-poor risk** | <br>S[1]<br>S[1] | <br>GNR<br>CO[2] | <br>GNR<br>GNR |
| **CR2** | S | S | GNR[3] |
| **Not in remission** | GNR | GNR | GNR |
| **Philadelphia positive ALL** | S | S | GNR |

References

1. Rowe et al. Blood 2006 (ASH plenary session)108:127, abstract no 2
2. Rowe and Goldstone Blood 110:2268-2275, 2007. Poor risk is defined as adverse cytogenetics, T-ALL with WCC>100, B-ALL with WCC>30, MRD positive after phase 2. Ideally this should be discussed with a member of the NCRI ALL group
3. Autografts, although inferior to chemotherapy in CR1 patients and inferior to allografts in CR2 patients may be justified when all other therapeutic options have been explored or the optimal therapy (eg chemotherapy) cannot be delivered

## Section 4

### *BSBMT Indications For Haematopoietic Stem Cell Transplantation In Lymphoma*

General Comments

a. An allogeneic stem cell transplant may be considered in any disease category where autologous stem cell harvesting has failed.
b. A MUD should be a 10/10, 8/8 or 9/10 allelic level match.

### *Hodgkin Lymphoma*

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **CR1** | GNR | GNR | GNR |
| **CR>1** | S[1] | CO[2] | CO[2] |
| **Relapse/ Primary Refractory**<br>- **Chemosensitive**<br>- **Chemorefractory** | S[1]<br>CO | CO[2]<br>CO[2] | CO[2]<br>CO[2] |
| **Relapse post autograft** | GNC | CO[3] | CO[3] |

References

1. Linch et al Lancet 1993; 341: 1050-1054, Schmitz et al Lancet 2002; 359: 2065-2071 2.
2. Patients considered at high risk of failing an auto in CR1 eg CR1<1 year, PET+ post salvage, less than PR post salvage, chemorefractory
3. Peggs Lancet 2005; 365: 1906-1908., Sureda JCO 2008; 26: 455-462

## Mantle Cell Lymphoma

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **CR1/PR1** | S[1] | CO[2] | CO[2] |
| **CR/PR>1** | CO[3] | CO[2] | CO[2] |
| **Chemorefractory** | GNR | D | D |
| **Relapse post autograft** | GNR | CO[3] | CO[3] |

References


1. Dreyling Blood 2005; 105:2677–2684
2. Khouri JCO 2003, Maris Blood 2004; 104: 3535, proposed NCRN trial (Rule et al)
3. Robinson Blood 2004; 104: 2322, Faulkner Blood 2004; 103: 428 -43


## Follicular Lymphoma

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **CR1/PR1** | GNR[1] | GNR | GNR |
| **CR/PR>1** | S[2] | CO[3] | CO[3] |
| **Chemorefractory** | GNR | D | D |
| **Relapse post autograft** | GNR | CO[4] | CO[4] |

References


1. Lenz Blood 2004; 104: 2667-2674
2. Schouten JCO 2003; 21: 3918-3927
3. van Besien Blood 1998; 92: 1832-1836, Morris Blood 2004; 104: 3865-3871, Robinson Blood 2002; 100: 4310-4316, Faulkner Blood
4. 2004; 103; 428-434
5. Morris Blood 2004; 104: 3865-387, Robinson Blood 2002; 100: 4310-4316

## DLBCL

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **CR1** | GNR[1] | GNR | GNR |
| **PR1 (sensitive to salvage)** | CO | CO | CO |
| **CR, PR>1** | S[2] | CO[3] | CO[4] |
| **Chemorefractory** | GNR | D | D |
| **Relapse post autograft** | GNR | CO[4] | CO[4] |

References


1. Cochrane database
2. Philip NEJM 1995
3. Chopra JCO 1992; 10: 1690-1695, Bierman JCO 2003; 21: 3744-3753
4. Morris Blood 2004; 104: 3865-387


## Peripheral T cell Lymphoma

| | **Autograft** | **Sibling transplant** | **MUD transplant** |
|---|---|---|---|
| **CR1** | CO[1] | CO[2] | CO[2] |
| **PR1 (sensitive to salvage_** | CO[1] | CO[2] | CO[2] |
| **CR/PR>1** | S | CO | CO |
| **Chemorefractory** | GNR | D | D |
| **Relapse post autograft** | GNR | CO[2] | CO[2] |

References


1. Reimer Blood 2005; 106;2074
2. Corradini JCO 2004; 22:2172-2176, Wulf BMT 2005; 36:271-273

# Section 5

## CLL

| | RIC Sib allograft | RIC VUD | Auto | UCB |
|---|---|---|---|---|
| **Very high risk CR1 (2)** | S | S | GNR | CT |
| **High risk CR2(3)** | S | S | CT | CT |
| **Others CR >2 (4)** | CO | CO | CO | CT |
| **Richters transformation** | S | S | GNR | CT |
| **T-PLL** | S | S | CO | CT |
| **B-PLL (5)** | CO | CO | CO | CT |

**Notes**

1. For most CLL patients, reduced intensity (RIC) conditioning is recommended however for some younger patients (<45 years) with very high risk disease and a matched sibling donor then standard intensity conditioning may be preferable (CO).
2. Very high risk CLL defined as CLL with >20% cells showing del. 17p or purine analogue refractory. These patients should be treated with p53 independent therapy, such as high dose methyl prednisolone and/or alemtuzumab to maximum response and then allografted if possible in CR1
3. High risk CLL defined according to EBMT criteria:1
   i. Relapse within 6 months of PA therapy
   ii. Relapse within 2 years of intensive therapy including PA/alkylator combinations, chemo-immunotherapy or autologous transplantation
4. Other indications. Includes patients not fulfilling criteria 2 or 3 who are in second or subsequent relapse with at least one other commonly recognised adverse features listed below:
   i. Bone marrow failure according to Binet criteria
   ii. Unmutated Vh genes (<98% germline or Vh3.21)
   iii. ZAP 70+ (>20%) iv. CD38+ (>7%)
   iv. v. Del 11q or trisomy 12
5. Approx 20% of cases of B-PLL actually mantle cell lymphoma and should be treated accordingly. B-PLL otherwise rare and should be treated on a case by case basis (CO)

## Abbreviations

S – Standard of care

CO – Clinical opinion

GNR – Generally not recommended CT – Only in context of clinical trial

CR1 or CR2 – Defined as first or second best response to therapy and includes either complete or partial remission as defined in NCI response criteria2. Patients with stable or progressive disease may respond to allogeneic transplantation but should be considered on a case by case basis (CO)

References

1. Dreger P, Corradini P, Kimby E, et al. Indications for allogeneic stem cell transplantation in chronic lymphocytic leukemia: the EBMT transplant consensus. Leukemia. 2007;21:12-17'
2. Cheson BD, Bennett JM, Grever M, et al. National Cancer Institute-sponsored Working Group guidelines for chronic lymphocytic leukemia: doi:10.1182/blood-2007-06-093906 Prepublished online Jan 23, 2008

## Section 6

## Indications for allograft in adult patients with aplastic anaemia

## Aplastic anaemia

| | Matched sibling | MUD | UCBT | Autologous |
|---|---|---|---|---|
| **Severe AA (SAA) < 50 yr** | S | S if failed IST and no sibling | CO | GNR |
| **SAA >50 yr** | S if failed IST | s if failed IST and no sibling | D | GNR |
| **Constitutional AA** | S | S if no sibling | CO | GNR |

IST = failed at least one course of IST (immunosuppressive therapy)

References


1. BCSH guidelines Brit. J. Haem. 2009; 147: 43
2. Bacigalupo et al. BBMT 2009; 15; issue 2, 5
3. Bacigalupo et al. Haematologica 2010 in press
4. Maury et al. Haematologica 2009; 94: 1312
5. Bacigalupo. EBMT data presented at ASBMT/Tandem Meeting 2010
6. Young NS, Bacigalupo A, Marsh J. BBMT 2010; 16; issue 1, S119

## Section 7

### Indications for Transplantation for Adults with Myelodysplastic Syndromes MDS

| IPSS score | Autograft | Sibling Allograft | VUD allograft | UCBT |
|---|---|---|---|---|
| **Low-Int-1** | GNR | CO* | CO* | D** |
| **Int-2, High** | GNR | S | S | D** |
| **t-MDS** | GNR | S | S | D** |

t-MDS: therapy related MDS

Reduced intensity conditioning protocols are recommended for patients aged 40-45 years or older, or in patients with pre-existing co- morbidities as defined using the HSCT co-morbidity index (HCT-CI)

*Allogeneic transplantation in patients with Low or Int-1 disease is generally considered at time of disease progression: progressive cytopenias and transfusion dependence, increasing blast counts, acquisition of adverse cytogenetic markers

**In view of the limited data on transplantation of adult patients with MDS using umbilical cord blood units, it is recommended that this should be performed within the confines of a clinical research protocol

## International Prognostic Scoring System

| | 0 | 0.5 | 1 | 1.5 | 2 |
|---|---|---|---|---|---|
| **% BM blasts** | <5 | 5-10 | | 11-20 | 21-30 |
| **Cytopenias** | 0-1 | 2-3 | | | |
| **Karyotype*** | Good | Intermediate | Poor | | |
| | | | | | |
| **Risk Category** | **Low risk** | **Int-1** | **Int-2** | **High risk** | |
| **Score** | 0 | 0.5-1 | 1.5-2 | ≥2.5 | |

*Good = normal, -Y, del(5q), del(20q)

Poor = complex(≥3 chromosome abnormalities) or chromosome 7 abnormalities
Intermediate = Changes not identified by the Good or Poor cytogenetic subgroups

References


1. Bowen, D., Culligan, D., Jowitt, S., Kelsey, S., Mufti, G., Oscier, D. & Parker, J. (2003). Guidelines for the diagnosis and therapy of adult myelodysplastic syndromes. Br J Haematol, 120, 187-200
2. Cutler, C.S., Lee, S.J., Greenberg, P., Deeg, H.J., Perez, W.S., Anasetti, C., Bolwell, B.J., Cairo, M.S., Gale, R.P., Klein, J.P., Lazarus, H.M., Liesveld, J.L., McCarthy, P.L., Milone, G.A., Rizzo, J.D., Schultz, K.R., Trigg, M.E., Keating, A., Weisdorf, D.J., Antin, J.H. & Horowitz, M.M. (2004). A decision analysis of allogeneic bone marrow transplantation for the myelodysplastic syndromes: delayed transplantation for low-risk myelodysplasia is associated with improved outcome. Blood, 104, 579-85
3. de Witte, T., Brand, R., van Biezen, A., Delforge, M., Biersack, H., Or, R., Meloni, G., Bandini, B., Sierra, J., Kroger, N., Gratwohl, A. & Niederwieser, D. (2006). The role of stem cell source in autologous hematopoietic stem cell transplantation for patients with myelodysplastic syndromes. Haematologica, 91, 750-6
4. Ho, A.Y., Pagliuca, A., Kenyon, M., Parker, J.E., Mijovic, A., Devereux, S. & Mufti, G.J. (2004). Reduced-intensity allogeneic haematopoietic stem cell transplantation for myelodysplastic syndrome and acute myeloid leukaemia with multilineage dysplasia using Fludarabine, Busulphan and Alemtuzumab (CAMPATH-1H)(FBC) conditioning. Blood
5. Martino, R., Iacobelli, S., Brand, R., Jansen, T., van Biezen, A., Finke, J., Bacigalupo, A., Beelen, D., Reiffers, J., Devergie, A., Alessandrino, E., Mufti, G.J., Barge, R., Sierra, J., Ruutu, T., Boogaerts, M., Falda, M., Jouet, J.P., Niederwieser, D. & de Witte, T.

(2006). Retrospective comparison of reduced-intensity conditioning and conventional high-dose conditioning for allogeneic hematopoietic stem cell transplantation using HLA-identical sibling donors in myelodysplastic syndromes. Blood, 108, 836-46

6. Scott, B.L., Sandmaier, B.M., Storer, B., Maris, M.B., Sorror, M.L., Maloney, D.G., Chauncey, T.R., Storb, R. & Deeg, H.J. (2006). Myeloablative vs nonmyeloablative allogeneic transplantation for patients with myelodysplastic syndrome or acute myelogenous leukemia with multilineage dysplasia: a retrospective analysis. Leukemia, 20, 128-35
7. Sorror, M.L., Maris, M.B., Storb, R., Baron, F., Sandmaier, B.M., Maloney, D.G. & Storer, B. (2005). Hematopoietic cell transplantation (HCT)specific comorbidity index: a new tool for risk assessment before allogeneic HCT. Blood, 106, 2912-9
8. Tauro S, Craddock C, Peggs, K, Begum G, Mahendra P, Cook G, Marsh J, Milligan D, Goldstone A, Hunter A, Khwaja A, Chopra R, Littlewood T, Peniket A, Parker A, Russell N, Jackson G, Hale G, Mackinnon S Allogeneic stem cell transplantation using a reduced intensity conditioning (RIC) regimen has the capacity to produce durable remissions and long term disease free survival in patients with high risk acute myeloid leukemia (AML) and myelodysplasia (MDS) J Clin Oncol (2005) 23:9387-93

# Section 8

## Indications for Haematopoietic Stem Cell Transplant for Solid Tumours. Ewing's sarcoma/PNET

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **High risk disease as part of initial treatment plan** | CO | GNR | GNR |
| **CR>1** | CO | GNR | BNR |

Notes and references:


1. Pediatr Blood Cancer 2007;49(2):115-116. This showed benefit to conventional multimodality therapy for children with high-risk disease cf conventional treatment
2. Pediatr Blood Cancer 2007;49(2):190-195. AL-Feris N et al. Does consolidation with autologous stem cell transplantation improve the outcome of children with metastatic or relapsed Ewing's sarcoma
3. Med J Aust 2009;190:121-5. Moore AS et al. Haematopoietic stem cell transplantation for children in Australia and New Zealand, 1998- 2006: a report of the Australasian Bone Marrow and Transplant Recipient Registry and the Australian and New Zealand children's haematology oncology group
4. Am J Clin Oncol 2005;28(3):301-9. Laurence V et al. Long-term follow up of high dose chemotherapy with autologous stem cell rescue in adults with Ewing tumour
5. J Clin Oncol 2006;24(24):3997-4002. Oberlin O et al. Impact of high dose busulfan plus melphalan as consolidation in metastatic Ewing tumours: a study by the societe Francaise des Cancers de l'Enfant. This is the basis of Euro-Ewing trial
6. J Cancer Res Clin Oncol 2007;133:1-11. Engelhardt M et al. High dose chemotherapy and autologous peripheral stem cell transplantation in adult patients with high-risk or advanced Ewing and soft tissue sarcoma

## Neuroblastoma

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **Poor-risk disease** | S | GNR | GNR |
| **CR>1** | CO | GNR | GNR |

Notes and references

1. Now part of BACUP information as an option in advanced disease
2. Cancer Chemother Pharmacol 1986;16:165-169. Hartmann O et al. Treatment of advanced neuroblastoma with high dose chemotherapy and autologous bone marrow transplantation
3. Bone Marrow Transplantation 1997;20:543-551. Cohn SL et al. Treatment of poor-risk neuroblastoma patients with high-dose chemotherapy and autologous peripheral stem cell rescue

## Germ Cell

| | Autograft (including tandem | Sibling transplant | MUD transplant |
|---|---|---|---|
| **CR>1** | S | GNR | GNR |
| **Refractory disease** | CO | GNR | GNR |

Notes and References:

1. Eur J Cancer 2008;44(2):237-241. Sammier C et al. Risk factors in germ cell tumour patients with relapse or progressive disease after first-line chemotherapy: evaluation of a prognostic score for survival after high dose chemotherapy
2. N Eng J Med 2007;357(4):340-348. Einhorn LH et al. High dose chemotherapy and stem cell rescue for metastatic germ cell tumours
3. Haematologica 2002;87:95-104. De Giorgi U et al. The status of high dose chemotherapy with haematopoietic stem cell transplantation in patients with germ cell tumour

## Soft tissue Sarcoma

| | Autograft | Sibling Transplant | MUD transplant |
|---|---|---|---|
| **CR1** | CO | GNR | GNR |

Notes and References:


1. Bone Marrow Transplantation 2004;34:37-41. Kasper B et al. High-dose chemotherapy with autologous peripheral blood stem cell transplantation for bone and soft tissue
2. Oncology 2005;68:2-3. Kasper B et al. Is there an indication for high-dose chemotherapy in the treatment of bone and soft-tissue sarcoma


## Breast

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **Adjuvant** | D | GNR | GNR |
| **Metastatic** | D | GNR | GNR |

## Ovary

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **Any indication** | D | GNR | GNR |

## Lung

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **Any indication** | D | GNR | GNR |

## Renal

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **Any indication** | GNR | D | D |

## Section 9:

### Myelofibrosis

| | Sibling Transplant | MUD Transplant | Reduced Intensity | Autograft |
|---|---|---|---|---|
| **Primary Myelofibrosis (for prognostic score see [1])**<br>• **Low Risk**<br>• **Intermediate Risk**<br>• **High Risk** | GNR CO (<45 yrs)<br>S (<45 yrs) | GNR CO (<45 yrs)<br>S (<45 yrs) | GNR CO (>45 yrs)<br>S (>45 yrs)<br>CO (<45 if clinically unfit) | GNR CO2 CO2 |
| **Secondary Myelfibrosis**<br>• **Post-PV MF**<br>• **Post-ET MF** | CO CO | CO CO | CO CO | GNR GNR |

[1] Dupriez B, Morel P, Demory J-L et al. (1996) Prognostic factors in agnogenic myeloid metaplasia: a report on 195 cases with a new scoring system. Blood 88, 1013-1018.

[2] Best results if 'rainy day' harvest obtained at diagnosis

## The Lille Scoring System

| No of adverse factors | Risk Group | Cases (%) | Median Survival |
|---|---|---|---|
| **0** | low | 47 | 93 |
| **1** | intermediate | 45 | 26 |
| **2** | high | 8 | 13 |

***Myeloablative regimen***


- Deeg HJ, Gooley TA, Flowers ME et al, (2003). Allogeneic hematopoietic stem cell transplantation for myelofibrosis. Blood, 102, 39123918.
- Guardiola P, Andersen JE, Bandini G et al. Allogeneic stem cell transplantation for agnogenic myeloid metaplasia, Blood 1999, 93, 28311838.
- Guardiola P, Andersen JE, Gluckman E. Myelofibrosis with myeloid metaplasia. (2000). N Eng J Med, 343, 659-660.


***Reduced intensity conditioning regimen***


- Rondelli D, Barosi G, Bacigalupo A et al (2005) Allogeneic hematopoietic stem-cell transplanatation with reduced-intensity conditioning in intermediate-or high risk patients with myelofibrosis with myeloid metaplasia. Blood, 105, 4115-4119.
- Merup M, Lazarevic V, Nahi H et al (2006) Different outcome of allogeneic transplantation in myelofibrosis using conventional or reduced- intensity conditioning regimens. Br J Haematol, 135, 367-373.

# Section 10

## Indications for Haematopoietic Stem Cell Transplant for Severe Autoimmune Diseases

Based on Ljungman et al. Allogeneic and autologous transplantation for haematological diseases, solid tumours and immune disorders: definitions and current practice in Europe 2008. Bone Marrow Transplantation 2009: submitted)

*All patients with the specified diseases must be deemed to have severe treatment resistant disease and sufficiently fit for transplant procedure as determined by appropriate multi-specialty review.

Autologous HSCT for other autoimmune disorders is considered as developmental.

### Multiple sclerosis

| | Sibling transplant | MUD transplant | Autograft |
|---|---|---|---|
| **Severe, resistant disease*** | GNR | GNR | CO |

References:


1. Saccardi, R., Kozak, T., Bocelli-Tyndall, C., Fassas, A., Kazis, A., Havrdova, E., Carreras, E., Saiz, A., Lowenberg, B., te Boekhorst, P.A., Gualandio, F., Openshaw, H., Longo, G., Pagliai, F., Massacesi, L., Deconink, E., Ouyang, J., Nagore, F.J., Besalduch, J., Lisukov, I.A., Bonini, A., Merelli, E., Slavino, S., Gratwohl, A., Passweg, J., Tyndall, A., Steck, A.J., Andolina, M., Capobianco, M., Martin, J.L., Lugaresi, A., Meucci, G., Saez, R.A., Clark, R.E., Fernandez, M.N., Fouillard, L., Herstenstein, B., Koza, V., Cocco, E., Baurmann, H. & Mancardi, G.L. (2006) Autologous stem cell transplantation for progressive multiple sclerosis: update of the European Group for Blood and Marrow Transplantation autoimmune diseases working party database. Mult Scler, 12, 814-823
2. Burt RK , Loh Y, Cohen B, Stefoski D, Balabanov R, Katsamakis G, Oyama Y, Russell EJ, Stern J, Muraro P, Rose J, Testori A, Bucha J, Jovanovic B, Milanetti F, Storek J, Voltarelli JC, Burns WH Autologous non-myeloablative haemopoietic stem cell transplantation in relapsing-remitting multiple sclerosis: a phase I/II study. Lancet Neurol. 2009 Mar;8(3):244-53.
3. Roccatagliata, L., Rocca, M., Valsasina, P., Bonzano, L., Sormani, M., Saccardi, R., Mancardi, G. & Filippi, M. (2007) The long-term effect of AHSCT on MRI measures of MS evolution: a five-year follow-up study. Mult Scler, 13, 1068-1070
4. Portaccio, E., Amato, M.P., Siracusa, G., Pagliai, F., Sorbi, S., Guidi, S., Bosi, A. & Saccardi, R. (2007) Autologous hematopoietic stem cell transplantation for very active relapsing-remitting multiple sclerosis: report of two cases. Mult Scler, 13, 676-678

## Systemic sclerosis

| | Sibling transplant | MUD transplant | Autograft |
|---|---|---|---|
| **Severe, resistant disease*** | D | GNR | CO |

References:


1. Vonk, M.C., Marjanovic, Z., van den Hoogen, F.H., Zohar, S., Schattenberg, A.V., Fibbe, W.E., Larghero, J., Gluckman, E., Preijers, F.W., van Dijk, A.P., Bax, J.J., Roblot, P., van Riel, P.L., van Laar, J.M. & Farge, D. (2008) Long-term follow-up results after autologous haematopoietic stem cell transplantation for severe systemic sclerosis. Ann Rheum Dis, 67, 98-104
2. Farge, D., Passweg, J., van Laar, J.M., Marjanovic, Z., Besenthal, C., Finke, J., Peter, H.H., Breedveld, F.C., Fibbe, W.E., Black, C., Denton, C., Koetter, I., Locatelli, F., Martini, A., Schattenberg, A.V., van den Hoogen, F., van de Putte, L., Lanza, F., Arnold, R., Bacon, P.A., Bingham, S., Ciceri, F., Didier, B., Diez-Martin, J.L., Emery, P., Feremans, W., Hertenstein, B., Hiepe, F., Luosujarvi, R., Leon Lara, A., Marmont, A., Martinez, A.M., Pascual Cascon, H., Bocelli-Tyndall, C., Gluckman, E., Gratwohl, A. & Tyndall, A. (2004) Autologous stem cell transplantation in the treatment of systemic sclerosis: report from the EBMT/EULAR Registry. Ann Rheum Dis, 63, 974-981.
3. Nash, R.A., McSweeney, P.A., Crofford, L.J., Abidi, M., Chen, C.S., Godwin, J.D., Gooley, T.A., Holmberg, L., Henstorf, G., LeMaistre, C.F., Mayes, M.D., McDonagh, K.T., McLaughlin, B., Molitor, J.A., Nelson, J.L., Shulman, H., Storb, R., Viganego, F., Wener, M.H., Seibold, J.R., Sullivan, K.M. & Furst, D.E. (2007) High-dose immunosuppressive therapy and autologous hematopoietic cell transplantation for severe systemic sclerosis: long-term follow-up of the US multicenter pilot study. Blood, 110, 1388-1396
4. Oyama, Y., Barr, W.G., Statkute, L., Corbridge, T., Gonda, E.A., Jovanovic, B., Testori, A. & Burt, R.K. (2007) Autologous non- myeloablative hematopoietic stem cell transplantation in patients with systemic sclerosis. Bone Marrow Transplant, 40, 549-555
5. Nash, R.A., McSweeney, P.A., Nelson, J.L., Wener, M., Georges, G.E., Langston, A.A., Shulman, H., Sullivan, K.M., Lee, J., Henstorf, G., Storb, R. & Furst, D.E. (2006) Allogeneic marrow transplantation in patients with severe systemic sclerosis: resolution of dermal fibrosis. Arthritis Rheum, 54, 1982-1986
6. Khorshid, O., Hosing, C., Bibawi, S., Ueno, N., Reveille, J., Mayes, M.D. & Champlin, R.E. (2004) Nonmyeloablative stem cell transplant in a patient with advanced systemic sclerosis and systemic lupus erythematosus. J Rheumatol, 31, 2513-2516
7. Loh, Y., Oyama, Y., Statkute, L., Verda, L., Quigley, K., Yaung, K., Barr, W., Jovanovic, B. & Burt, R.K. (2007) Non-myeloablative allogeneic hematopoietic stem cell transplantation for severe systemic sclerosis: graft-versus-autoimmunity without graft-versus-host disease? Bone Marrow Transplant, 39, 435-437

## Systemic lupus erythematosus

| | Sibling transplant | MUD transplant | Autograft |
|---|---|---|---|
| **Severe, resistant disease*** | D | GNR | CO |

References:


1. Burt, R.K., Traynor, A., Statkute, L., Barr, W.G., Rosa, R., Schroeder, J., Verda, L., Krosnjar, N., Quigley, K., Yaung, K., Villa Bs, M., Takahashi, M., Jovanovic, B. & Oyama, Y. (2006b) Nonmyeloablative hematopoietic stem cell transplantation for systemic lupus erythematosus. Jama, 295, 527-535
2. Jayne, D., Passweg, J., Marmont, A., Farge, D., Zhao, X., Arnold, R., Hiepe, F., Lisukov, I., Musso, M., Ou-Yang, J., Marsh, J., Wulffraat, N., Besalduch, J., Bingham, S.J., Emery, P., Brune, M., Fassas, A., Faulkner, L., Ferster, A., Fiehn, C., Fouillard, L., Geromin, A., Greinix, H., Rabusin, M., Saccardi, R., Schneider, P., Zintl, F., Gratwohl, A. & Tyndall, A. (2004) Autologous stem cell transplantation for systemic lupus erythematosus. Lupus, 13, 168-176
3. Lu, Q., Lu, L., Niu, X., Guo, Y., Parino, G.R. & Liu, D. (2006) Non-myeloablative allogeneic stem cell transplant in a patient with refractory systemic lupus erythematosus. Bone Marrow Transplant, 37, 979-981
4. Khorshid, O., Hosing, C., Bibawi, S., Ueno, N., Reveille, J., Mayes, M.D. & Champlin, R.E. (2004) Nonmyeloablative stem cell transplant in a patient with advanced systemic sclerosis and systemic lupus erythematosus. J Rheumatol, 31, 2513-2516


## Rheumatoid arthritis

| | Sibling transplant | MUD transplant | Autograft |
|---|---|---|---|
| **Severe, resistant disease*** | GNR | GNR | CO |

References:


1. Snowden, J.A., Kapoor, S. & Wilson, A.G. (2008) Stem cell transplantation in rheumatoid arthritis. Autoimmunity, 2008 Oct 28:1. [Epub ahead of print]
2. Snowden, J.A., Passweg, J., Moore, J.J., Milliken, S., Cannell, P., Van Laar, J., Verburg, R., Szer, J., Taylor, K., Joske, D., Rule, S., Bingham, S.J., Emery, P., Burt, R.K., Lowenthal, R.M., Durez, P., McKendry, R.J., Pavletic, S.Z., Espigado, I., Jantunen, E., Kashyap, A., Rabusin, M., Brooks, P., Bredeson, C. & Tyndall, A. (2004) Autologous hemopoietic stem cell transplantation in severe rheumatoid arthritis: a report from the EBMT and ABMTR. J Rheumatol, 31, 482-488.

## Crohn's disease

| | Sibling transplant | MUD transplant | Autograft |
|---|---|---|---|
| **Severe, resistant disease*** | GNR | GNR | CO |

References:

1. Oyama, Y., Craig, R.M., Traynor, A.E., Quigley, K., Statkute, L., Halverson, A., Brush, M., Verda, L., Kowalska, B., Krosnjar, N., Kletzel, M., Whitington, P.F. & Burt, R.K. (2005) Autologous hematopoietic stem cell transplantation in patients with refractory Crohn's disease. Gastroenterology, 128, 552-563

2. Cassinotti A, Annaloro C, Ardizzone S, Onida F, Della Volpe A, Clerici M, Usardi P, Greco S, Maconi G, Porro GB, Deliliers GL Autologous haematopoietic stem cell transplantation without CD34+ cell selection in refractory Crohn's disease. Gut. 2008 Feb;57(2):211-7

## Immune cytopenias

| | Sibling transplant | MUD transplant | Autograft |
|---|---|---|---|
| **Severe, resistant ITP, AIHA, Evans** | D | D | D |

References:

1. Passweg, J.R., Rabusin, M., Musso, M., Beguin, Y., Cesaro, S., Ehninger, G., Espigado, I., Iriondo, A., Jost, L., Koza, V., Lenhoff, S., Lisukov, I., Locatelli, F., Marmont, A., Philippe, P., Pilatrino, C., Quartier, P., Stary, J., Veys, P., Vormoor, J., Wahlin, A., Zintl, F., Bocelli-Tyndall, C., Tyndall, A. & Gratwohl, A. (2004) Haematopoetic stem cell transplantation for refractory autoimmune cytopenia. Br J Haematol, 125, 749-755
2. Urban, C., Lackner, H., Sovinz, P., Benesch, M., Schwinger, W., Dornbusch, H.J. & Moser, A. (2006) Successful unrelated cord blood transplantation in a 7-year-old boy with Evans syndrome refractory to immunosuppression and double autologous stem cell transplantation. Eur J Haematol, 76, 526-530

## Chronic inflammatory demyelinating polyneuropathy (CIDP)

| | Autograft | Sibling transplant | MUD transplant |
|---|---|---|---|
| **Severe, resistant disease*** | D | GNR | GNR |

References:


1. Oyama Y, Sufit R, Loh Y, Statkute L, Yaung K, Quigley K, Gonda E, Spahovic D, Bronesky D, Burt RK. Nonmyeloablative autologous hematopoietic stem celltransplantation for refractory CIDP. Neurology. 2007 Oct 30;69(18):1802-3
2. Vermeulen, M. & Van Oers, M.H. (2002) Successful autologous stem cell transplantation in a patient with chronic inflammatory demyelinating polyneuropathy. J Neurol Neurosurg Psychiatry, 72, 127-128
3. Mahdi-Rogers M., Kazmi M., Ferner R., Hughes R.A.C., Renaud S., Steck A., Fuhr P., Halter J., Gratwohl A., Tyndall A. Autologous peripheral blood stem cell transplantation for chronic acquired demyelinating neuropathy Journal of the Peripheral Nervous System 2009 in press.