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Review Article

Haematopoietic Stem Cell Mobilisation Regimens and Graft Composition in Autologous Transplantation

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Abstract

Background: Autologous transplantation needs a graft collected by apheresis after mobilisation, and the regimen determines whether enough cells are obtained, and at what cost.

Objective: To review mobilisation regimens, the definition of poor mobilisation, and whether graft composition beyond CD34 count predicts anything.

Methods: Narrative review of randomised trials, consensus documents and comparative cohorts.

Findings: Plerixafor raised the proportion meeting the collection target from 34.4% to 71.6% in myeloma and from 20% to 59% in lymphoma; motixafortide reached 92.5% against 26.2%. Yet median neutrophil engraftment was 12 days in both arms of that trial. Chemomobilisation also collects more cells without changing engraftment, and CD34 subsets predict worse than total CD34 dose.

Conclusions: The gains these trials establish are logistical. Graft composition beyond CD34 count remains hypothesis-generating.

Keywords: mobilisation; plerixafor; CD34; autologous transplantation; graft composition

Introduction

An autologous transplant begins with a collection, and a collection that fails delays or prevents the transplant. Mobilisation is therefore a logistical problem before it is a biological one, and much of the literature is best read with that in mind.

The variables are few and well defined. Granulocyte colony-stimulating factor may be given alone or after chemotherapy; a CXCR4 antagonist may be added, either from the outset or when the peripheral blood CD34 count predicts failure; and the graft is characterised by its CD34 content, conventionally against a threshold. What has changed in twenty years is not the framework but the availability of agents that rescue patients who would previously have failed.

This review considers what those agents achieve, how poor mobilisation should be defined, and whether anything in the graft beyond the CD34 count is worth measuring.

Materials and Methods

Records were retrieved from Crossref, OpenAlex, Europe PMC and publisher pages for the terms *stem cell mobilisation*, *plerixafor*, *motixafortide*, *CD34*, *poor mobilizer* and *graft composition*. Priority was given to randomised trials and consensus documents. Every bibliographic record was confirmed at source, and quantitative values were taken from the source rather than from secondary citation.

The CD34 threshold and what it rests on

The dose convention derives from engraftment kinetics in large early series. In 692 patients, the CD34 content of the product was the single most powerful mediator of both neutrophil and platelet recovery, each at $p = 0.0001$, with a median of 9 days to a neutrophil count of $0.5 \times 10^9/l$; the authors could not define a minimum threshold but concluded that at least 5.0×10^6 CD34+ cells/kg

appeared optimal for rapid recovery [1]. Factors influencing collection and engraftment were characterised in parallel [2], and the long-term significance of CD34 dose was examined subsequently [3].

Two things follow that are often conflated. A minimum dose is required for reliable engraftment; and above that dose, more cells speed platelet recovery to a diminishing degree. Neither supports collecting indefinitely.

Growth factor alone against chemomobilisation

Chemotherapy plus growth factor collects more cells. A randomised trial in relapsed or refractory lymphoma found higher CD34 yields with combined chemotherapy and G-CSF than with G-CSF alone, at a median of 7.2 against 2.5×10^6 cells/kg ($p = 0.004$), and stated the result plainly: this did not affect engraftment, with median neutrophil recovery 11 days in both arms and platelet recovery differing by a day [4]. A retrospective comparison of 716 myeloma patients found fewer apheresis sessions with cyclophosphamide, two against four ($p = 0.001$) [5], and a multicentre study addressed the same question in the era of novel agents [6].

So the case for chemomobilisation is that it collects faster, not that it produces a better transplant.

CXCR4 antagonists

Two randomised placebo-controlled trials established plerixafor. In myeloma, 106 of 148 patients (71.6%) met the primary endpoint with plerixafor against 53 of 154 (34.4%) with placebo, $p < 0.001$; 54% of plerixafor-treated patients reached target after one apheresis, whereas 56% of placebo-treated patients required four [7]. In non-Hodgkin lymphoma, 89 of 150 (59%) met the endpoint against 29 of 148 (20%), $p < 0.001$ [8]. European compassionate-use data across 13 countries and 580 poor mobilisers found collection yields higher in myeloma than in lymphoma, with 81.6% against 64.8% exceeding 2.0×10^6 CD34+ cells/kg [9].

Motixafortide extended the effect. In a randomised phase III trial, 92.5% met the primary endpoint against 26.2% with placebo (odds ratio 53.3, 95% CI 14.12–201.33, $p < 0.0001$), and 88.8% did so in a single apheresis against 9.5% (odds ratio 118.0, 95% CI 25.36–549.35). Median yield in one apheresis day was 10.8 against 2.25×10^6 cells/kg. Median time to neutrophil engraftment was 12 days in both arms, and median time to platelet engraftment was 18 days with motixafortide against 17 with placebo [10].

That last sentence is the one worth pausing on. A more than threefold difference in collection success produced no difference in engraftment.

Predicting and pre-empting failure

Because rescue is possible, prediction has value. A definition of the poor mobiliser was proposed by an Italian working group [11], its predicted and proven incidence compared [12], and the incidence, risk factors and consequences characterised in a single-centre series [13]. Countermeasures have been reviewed [14].

The strongest predictor is the peripheral blood CD34 count before apheresis, which is what the European position statement identifies and what makes pre-emptive intervention possible [15]. An algorithm using the day-4 peripheral CD34 count and the collection target to choose between continuing G-CSF and adding plerixafor completed collection within the predicted number of sessions in 91% of patients [16]. Just-in-time rescue has been reported in Hodgkin lymphoma [17] and after failing chemomobilisation [18], and the approaches have been reviewed [19]. Consensus recommendations address the same choices [20].

Drug exposure matters too: lenalidomide reduces CD34 yield and increases apheresis number, with the effect worsening with duration of exposure, and the recommendation is to collect within six months of starting it [21].

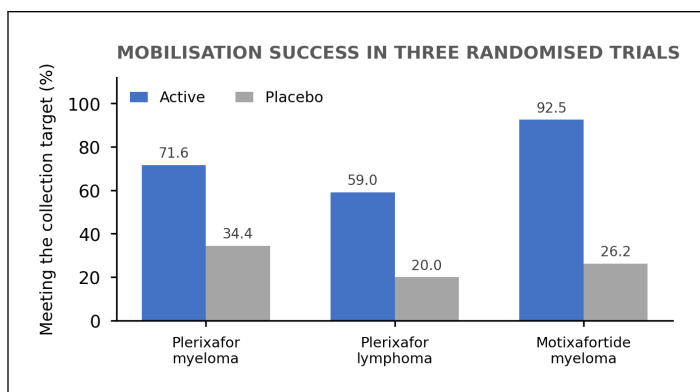


Figure 1: Proportion of patients meeting the collection target with a CXCR4 antagonist against placebo, across three randomised trials. Each trial's endpoint definition differs, so the bars are comparable in direction rather than in magnitude. Data from DiPersio et al. [7,8] and Crees et al. [10].

Cost analysis favours the chemotherapy-free approach in one Italian model, at 8039.85 against 9238.44 per patient [22], though these are model outputs rather than observed proportions.

Graft composition beyond CD34

Here the literature promises more than it delivers. CD34 subsets were compared directly against total CD34 dose and found inferior as predictors of engraftment [23] — a title that states its own conclusion. A substantial body of work from one group associates the infused autograft absolute lymphocyte count with day-15 lymphocyte recovery and with clinical outcome in lymphoma [24], natural killer cell content with lymphocyte recovery [25], the lymphocyte-to-monocyte ratio with survival in T-cell lymphoma [26], a natural killer to monocyte ratio with survival [27], and absolute immune effector numbers with survival generally [28], including in double- and triple-hit lymphoma [29].

The consistency is notable and so is the provenance. These are largely retrospective analyses with data-derived cut-offs from one centre, in which disease status and prior therapy confound both the graft composition and the outcome. Treat them as hypothesis-generating.

Table 1: Randomised placebo-controlled mobilisation trials and their endpoints.			
Trial	Population	Primary endpoint met	Statistic
Plerixafor [7]	Multiple myeloma	106/148 (71.6%) vs 53/154 (34.4%)	p < 0.001
Plerixafor [8]	Non-Hodgkin lymphoma	89/150 (59%) vs 29/148 (20%)	p < 0.001
Motixafortide [10]	Multiple myeloma	92.5% vs 26.2%	OR 53.3 (14.12-201.33)
Motixafortide, one apheresis [10]	Multiple myeloma	88.8% vs 9.5%	OR 118.0 (25.36-549.35)
G-CSF vs chemomobilisation [4]	Relapsed lymphoma	Median 2.5 vs 7.2 x 10 ⁶ /kg collected	p = 0.004; engraftment unchanged

Discussion

Three conclusions follow. First, the randomised evidence for CXCR4 antagonists is strong and its endpoint is a collection target, not a patient outcome. Second, the same holds for chemomobilisation, which collects more cells without changing engraftment. Third, no measure of graft composition beyond total CD34 dose has been shown to predict outcome in a way that survives independent replication.

This is a narrative review without systematic search or risk-of-bias assessment. Several quantitative results, including engraftment data from the plerixafor trials, could not be confirmed at source and are therefore not reported.

Conclusion

Mobilisation practice is now well supplied with effective agents, and the choice between them is largely one of cost, scheduling and institutional pattern rather than of transplant outcome. The peripheral blood CD34 count before apheresis remains the most useful predictor and the basis for pre-emptive rescue. Beyond total CD34 dose, graft composition has not been shown to matter, and the literature associating lymphocyte or natural killer content with survival should be read as a hypothesis awaiting a

prospective test. Studies should report the mobilisation regimen, the peripheral CD34 trigger used, the collection target and the number of apheresis sessions alongside any outcome claim.

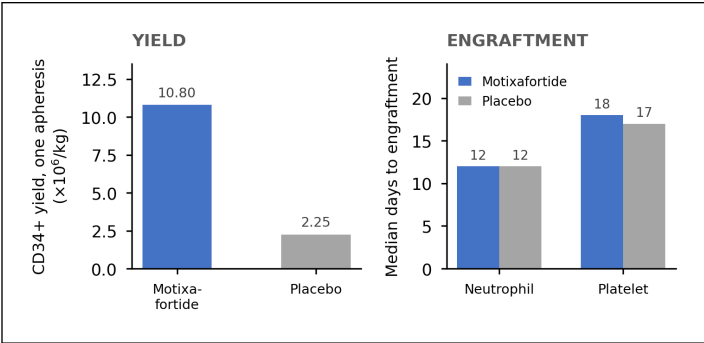


Figure 2: Collection yield against engraftment in the motixafortide trial. A nearly fivefold difference in median CD34 yield produced identical median neutrophil engraftment and a one-day difference in platelet engraftment favouring placebo. Data from Crees et al. [10].

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Conflict of Interest

The authors declare that they have no competing interests relevant to the content of this review.

Ethics Statement

This article reviews previously published studies and contains no new studies with human participants or animals performed by any of the authors. Ethical approval was therefore not required.

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