National Horizon Scanning Centre

Plerixafor (Mozobil) for stem-cell mobilisation in multiple myeloma

December 2007

This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Plerixafor (Mozobil) for stem-cell mobilisation in multiple myeloma

Target group
- Multiple myeloma (MM) – undergoing autologous transplantation

Technology description
Plerixafor (Mozobil, AMD 3100) is a first in class CXCR4 antagonist that mobilises stem cells from the bone marrow increasing their numbers in peripheral blood. Plerixafor blocks the CXCR4 chemokine receptor and its cognate ligand SDF-1α, which are involved in the retention of stem cells in bone marrow. As plerixafor is a release factor and not a growth factor it does not initiate differentiation of haematopoietic stem cells.

Plerixafor is administered by subcutaneous injection at 240 µg/kg in combination with a granulocyte-colony stimulating factor (G-CSF) prior to autologous stem cell transplant.

Plerixafor is also in clinical trials for stem cell mobilisation in non-Hodgkin’s lymphoma.

Innovation and/or advantages
Plerixafor is the first in class and has the potential to reduce the number of apheresis sessions required and increase the number of patients reaching minimum cell-yield target who can proceed to transplantation.

Developer
Genzyme Therapeutics.

Place of use
- Home care e.g. home dialysis
- Secondary care e.g. general, non-specialist hospital
- General public e.g. over the counter
- Community or residential care e.g. district nurses, physio
- Tertiary care i.e. specialist treatment centres
- Primary care e.g. used by GPs or practice nurses
- Emergency care e.g. paramedic services, trauma care
- Other:

Availability, launch or marketing dates, and licensing plans:
The company anticipate a licence application in the EU in 2008. Plerixafor has been granted orphan drug status in the EU and US.

NHS or Government priority area:
This topic is relevant to the NHS Cancer Plan.

Relevant guidance
Clinical need and burden of disease

In 2005 there were 3,353 new cases of MM registered in England and Wales, with 2,181 deaths. In 2006 there were 727 autologous peripheral blood stem cell transplants undertaken in patients with MM in the UK. It is unclear what proportion of patients undergoing autologous transplantation would benefit from plerixafor.

Existing comparators and treatments

- Recombinant human granulocyte-colony-stimulation factor (G-CSF): used either alone prior to autologous transplantation or after myelosuppressive chemotherapy.
  - Filgrastim (Neupogen)
  - Lenograstim (Granocyte)

Efficacy and safety

There are many published or registered case series and/or small non-randomised, open label trials of plerixafor, but only 3 randomised trials:

<table>
<thead>
<tr>
<th>Trial name or code</th>
<th>AMD3100-3102; NCT00103662 &amp; 476294 Phase III; with long-term extension trial</th>
<th>AMD3100-C201; NCT00396266 Phase II (MM or NHL)</th>
<th>First trial in patients (MM or NHL)</th>
</tr>
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<tbody>
<tr>
<td>Sponsor</td>
<td>Genzyme</td>
<td>Genzyme</td>
<td>-</td>
</tr>
<tr>
<td>Status</td>
<td>Recruitment complete, in follow-up; interim results</td>
<td>Ongoing – no longer recruiting</td>
<td>Published¹</td>
</tr>
<tr>
<td>Location</td>
<td>USA, Canada, Europe</td>
<td>Canada</td>
<td>USA</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, double-blind, placebo-controlled</td>
<td>Open-label, uncontrolled</td>
<td>Randomised, cross-over, proof-of-concept</td>
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<tr>
<td>Participants in trial</td>
<td>n=302; MM; undergoing haematopoietic stem cell transplant. Randomised to G-CSF (10 µg/kg/day) with plerixafor (240 µg/kg) or G-CSF with placebo.</td>
<td>N=23; MM or non-Hodgkin’s lymphoma (NHL); undergoing autologous transplant. Plerixafor (240 µg/kg) and G-CSF (10 µg/kg/day) prior to apheresis for up to 5 consecutive days.</td>
<td>N=25; MM or NHL in complete or partial remission; undergoing autologous transplant. Randomised to G-CSF with plerixafor or G-CSF alone; 2-week washout before cross-over.</td>
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<td>Follow-up</td>
<td>12 months; with additional 3-year long-term follow-up.</td>
<td>12 months following transplant</td>
<td>-</td>
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<tr>
<td>Primary outcome</td>
<td>Target mobilisation threshold of ≥6 million CD34+ cells/kg in ≤2 apheresis sessions.</td>
<td>Safety</td>
<td>Average CD34+ cells/kg per day of apheresis; total number of CD34+ cells/kg.</td>
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<tr>
<td>Secondary outcomes</td>
<td>Target mobilisation threshold of ≥6 million CD34+ cells/kg in ≤4 sessions; ≥2 million CD34+ cells/kg in ≤4 apheresis sessions. Engraftment of cells; graft durability to 100 days. Disease-free survival and overall survival.</td>
<td>≥2-fold increase in circulating CD34+ cells; time to engraftment of stem cells.</td>
<td>≥ 2 million CD34+ cells/kg collected</td>
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<tr>
<td>Key results</td>
<td>Primary threshold reached in 72% of plerixafor group vs. 34% G-CSF alone (p&lt;0.0001).</td>
<td>-</td>
<td>More CD34+ cells were collected after plerixafor with G-CSF, than with G-CSF alone.</td>
</tr>
</tbody>
</table>
Median number of days to achieve primary threshold was 1 day for plerixafor group vs. 4 days for G-CSF alone. In 84% of cases plerixafor with G-CSF produced a daily increase in CD34+ cells/kg of more than 50%. Patients with NHL mobilised a median of 4.4-fold more cells with plerixafor.

<table>
<thead>
<tr>
<th>Expected reporting date</th>
<th>Results to be presented to American Society of Hematology in Dec 2007.</th>
<th>Trial commenced January 2005</th>
<th>N/A</th>
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<tbody>
<tr>
<td>Adverse effects</td>
<td>Plerixafor was well tolerated; most common adverse effects were mild gastrointestinal effects and injection site redness.</td>
<td>-</td>
<td>No serious adverse events were felt related to plerixafor. Most common milder adverse events associated with plerixafor were diarrhoea, injection site redness and nausea.</td>
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</table>

### Estimated cost and cost impact

The cost of plerixafor is not yet known. The cost of available G-CSF is:

<table>
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<tr>
<th>Drug</th>
<th>Dose</th>
<th>Cost of course(^a)</th>
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<tr>
<td>Filgrastrim</td>
<td>1 MU/kg daily for 5-7 days</td>
<td>£545 to £763</td>
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<tr>
<td>Lenograstim</td>
<td>1.28 MU/kg for 4-6 days</td>
<td>£815 to ££1,223</td>
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</table>

### Potential or intended impact – speculative

**Patients**
- ☑ Reduced morbidity: Increased numbers of patients reaching cell yield target who may proceed to transplantation
- ☐ Quicker, earlier or more accurate diagnosis or identification of disease
- ☑ Reduced mortality or increased survival: Increased numbers of patients reaching cell yield target who may proceed to transplantation
- ☑ Improved quality of life for patients and/or carers: Fewer transfusions
- ☐ Other: Non identified

**Services**
- ☐ Increased use
- ☑ Decreased use: reduced numbers of blood transfusions and hospital days
- ☐ Service reorganisation required
- ☐ Staff or training required
- ☐ Other: Non identified

**Costs**
- ☐ Increased unit cost compared to alternative
- ☑ New costs: Additional mobilisation agent
- ☐ Increased costs: more patients coming for treatment
- ☑ Savings: Reduced supportive care costs as reduced numbers of blood transfusions and hospital days
- ☐ Increased costs: capital investment needed
- ☐ Other: Non identified

\(^a\) Costs from BNF 53, March 2007. Average weight adult 67.5kg.
References


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