Moxetumomab pasudotox is a new drug to treat hairy cell leukaemia. Hairy cell leukaemia is a type of cancer in which the bone marrow makes too many white blood cells. Moxetumomab pasudotox is delivered straight into the blood and may offer a new treatment option for people whose cancer has returned after their previous treatment.
TARGET GROUP

- Hairy cell leukaemia (HCL): treatment-refractory, stage III or IV - third line.

TECHNOLOGY

DESCRIPTION

Moxetumomab pasudotox (CAT-8015; GCR-8015; HA22) is an anti-CD22 recombinant immunotoxin consisting of an engineered toxin fused with a disulphide-linked antibody fragment, which targets the CD22 receptor and minimises non-targeted toxicity. It is intended for adults with treatment refractory HCL (stage III or IV) after two previous treatments with purine analogues (e.g. cladribine and pentostatin) have failed. In the phase III clinical trial, moxetumomab pasudotox monotherapy is administrated by intravenous (IV) infusion at 40µg/kg on days 1, 3 and 5 of each 28 day cycle until disease progression.¹

Moxetumomab pasudotox does not currently have a Marketing Authorisation in the EU for any indication.

Moxetumomab pasudotox is also in phase II development for acute lymphoblastic leukaemia.

INNOVATION and/or ADVANTAGES

If licensed, moxetumomab pasudotox will offer an additional treatment option for patients with stage III or IV hairy cell leukaemia who have failed their initial lines of treatment.

DEVELOPER

AstraZeneca UK Ltd.

AVAILABILITY, LAUNCH OR MARKETING

Moxetumomab pasudotox is in phase III clinical trials.

PATIENT GROUP

BACKGROUND

HCL is an indolent and rare type of chronic lymphocytic leukaemia (CLL). CLL is characterised by the accumulation of resting malignant B cells in peripheral blood and the presence of proliferating malignant B cells in the lymph nodes, spleen and bone marrow.² The progressive accumulation of monoclonal B lymphocytes leads to leucocytosis, lymphadenopathy, hepatosplenomegaly, anaemia, thrombocytopenia, neutropenia, bone marrow failure, recurrent infections and systemic symptoms (such as fatigue, weight loss, night sweats).³ In HCL, the malignant B lymphocytes can be seen to have hair-like projections, accounting for the name.⁴
**CLINICAL NEED and BURDEN OF DISEASE**

HCL is rare, accounting for approximately 3% of all leukaemia cases. Around 220 people in the UK are diagnosed with HCL each year. HCL occurs mostly in people aged 40-60 and is more common in men than in women. Based on a small number of patients from one area of England, it is estimated that 90% of patients with HCL will survive at least 10 years after diagnosis. Recurrence of disease is reported in 24-33%, and 42-48% of patients at 5 and 10 years after diagnosis, respectively. It has been reported that between 2% and 24% of patients with HCL will not achieve a sufficient response following initial treatment with purine analogues.

In England, there were 186 new cases of HCL (ICD-10 C91.4) recorded in 2014. In 2014-15, there were 1,599 hospital admissions in England for HCL, resulting in 1,656 finished consultant episodes and 855 bed days. In 2014, there were 34 deaths from HCL in England and Wales.

**PATIENT PATHWAY**

**RELEVANT GUIDANCE**

**NICE Guidance**

**NHS England Policies and Guidance**

**Other Guidance**
- European Society for Medical Oncology. Hairy cell leukaemia: ESMO Clinical practice guidelines for diagnosis, treatment and follow-up. 2015.

**CURRENT TREATMENT OPTIONS**

HCL develops slowly and treatment is not indicated for asymptomatic patients. However, guidelines recommend that untreated patients should be closely monitored with a complete history, physical examination, and full blood cell (including white cell differential) every 3–6 months.

The purine analogues cladribine or pentostatin are recommended for the first line treatment of symptomatic HCL. Interferon alpha is recommended for patients with extreme cytopenia.
For patients who relapse 12-18 months after initial treatment, re-treatment with the same purine analogues is recommended. If the relapse occurs less than 12 months after initial treatment, rituximab (unlicensed for this indication) is recommended in combination with further purine analogue treatment for second and subsequent line treatment\textsuperscript{12,13}.

**EFFICACY and SAFETY**

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT01829711, 130106, 13-C-0106, CD-ON-CAT-8015-1053; moxetumomab pasudotox; phase III.</th>
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<tbody>
<tr>
<td>Sponsor</td>
<td>MedImmune LLC.</td>
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<tr>
<td>Status</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry\textsuperscript{1}, manufacturer.</td>
</tr>
<tr>
<td>Location</td>
<td>EU (incl UK), USA, Canada, Israel and Norway.</td>
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<tr>
<td>Design</td>
<td>Non-randomised, uncontrolled.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=77 (planned); aged ≥18 yrs; hairy cell leukaemia; prior treatment with 2 purine analogues, or 1 course of purine analogue and 1 of either rituximub or a BRAF inhibitor; Eastern Cooperative Oncology Group (ECOG) performance status ≤2.</td>
</tr>
<tr>
<td>Schedule</td>
<td>Moxetumomab pasudotox 40µg/kg IV at on days 1, 3 and 5 of each 28 day cycle.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment for a maximum of 6 cycles (6 mths) or until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td>Primary outcome/s</td>
<td>Rate of complete response.</td>
</tr>
<tr>
<td>Secondary outcome/s</td>
<td>Overall response rate, relapse free survival, progression free survival, time to response, safety, pharmacokinetics. No quality of life measurement included in trial outcomes.</td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>Study completion date reported as May 2017.</td>
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</table>

**ESTIMATED COST and IMPACT**

**COST**

The cost of moxetumomab pasudotox is not yet known.

**IMPACT - SPECULATIVE**

**Impact on Patients and Carers**

- Reduced mortality/increased length of survival
- Other

**Impact on Health and Social Care Services**

- Increased use of existing services
- Decreased use of existing services
- Re-organisation of existing services
- Need for new services
- Other

**Impact on Costs and Other Resource Use**

- None identified
<table>
<thead>
<tr>
<th>Increased drug treatment costs</th>
<th>Reduced drug treatment costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other increase in costs</td>
<td>Other reduction in costs</td>
</tr>
<tr>
<td>Other: <strong>uncertain unit cost compared to existing treatments</strong></td>
<td>None identified</td>
</tr>
</tbody>
</table>

**Other Issues**

| Clinical uncertainty or other research question identified | None identified |

**REFERENCES**


