TITLE: Brentuximab for Refractory CD30+ Hodgkin’s Lymphoma: Clinical and Cost-Effectiveness

DATE: 23 April 2013

RESEARCH QUESTIONS

1. What is the clinical effectiveness of brentuximab for patients with refractory CD30+ Hodgkin’s lymphoma?

2. What is the cost-effectiveness of brentuximab for patients with refractory CD30+ Hodgkin’s lymphoma?

KEY MESSAGE

Six non-randomized studies were identified regarding the clinical effectiveness of brentuximab for patients with refractory CD30+ Hodgkin’s lymphoma. No economic evaluations were identified.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 3), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by publication type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and April 12, 2013. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and economic evaluations.

Six non-randomized studies were identified regarding the clinical effectiveness of brentuximab vedotin for patients with refractory CD30+ Hodgkin’s lymphoma. No relevant randomized controlled trials or economic evaluations were identified. Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Overall, evidence from six non-randomized studies suggests that brentuximab vedotin was an effective treatment1-6 for patients with CD30+ refractory or relapsed Hodgkin’s Lymphoma (HL) and was rated as mildly or moderately toxic.1,2,6 Tumor regression2,6 and objective response rates1-5 were reported in most patients, while complete response was observed in some patients within all of the studies.1-6 When reported, the duration of response was between 84 and 9.76 months, time to response was reported in only one study at 8.1 months3, and progression-free survival ranged from 5.1 to 7.8 months.1,3,5 Overall survival was either not reported1,2,4-6 or not achieved3 in the identified studies. The most common adverse events were peripheral sensory neuropathy, fatigue, nausea, diarrhea, arthralgia, pyrexia, cough, dyspnea, and neutropenia.2,3,5,6 Table 1 includes the details pertaining to the patient and study characteristics, patient responses, toxicities, and adverse events. Conclusions of note regarding the use of brentuximab vedotin included:

- In one quarter of patients refractory to conventional salvage therapies, brentuximab vedotin was an effective bridge to allogeneic transplantation with the best responses observed after four doses.1
- It appeared to be be potentially useful for selected relapsing HL patients after receiving allogeneic stem cell transplantation.3
- It was effective in heavily pre-treated CD30+ malignancies.4
- Objective responses were observed in 75% patients with relapsed or refractory HL after autologous stem-cell transplantation with complete responses approaching 2 years in some patients.5
- Complete responses,1-6 tumor regression2,6 and durable remissions2,5 were also observed.

No relevant cost-effectiveness information was identified.
### Table 1: Responses to Brentuximab Vedotin Treatment in Patients with Hodgkin's Lymphoma

<table>
<thead>
<tr>
<th>Cited Studies</th>
<th>Patient and Study Characteristics</th>
<th>Patient Responses</th>
<th>Toxicity</th>
<th>Most Common AEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fanale et al, 2012</td>
<td>Pts: ● n=38 with HL; n= 5 with SALCL, n=1 with PTCL ● received drug on days 1, 8, 15 of each 28 day cycle ● doses ranging from 0.4 – 1.4 mg/kg ● MTD was 1.2 mg/kg Study: ● Phase I DE</td>
<td>CR (%): 34 OS (mo): NR TR (%): 85 ORR (%): 59 TIR (wks): NR DR (mo): NA TR (wks): NR PFS (mo): NR</td>
<td>Mild to moderate</td>
<td>PSN fatigue nausea diarrhea arthralgia pyrexia</td>
</tr>
<tr>
<td>Gopal et al, 2012</td>
<td>Pts: ● n=25 with n=24 evaluable ● HL with recurrent disease &gt;100 days after alloSCT ● no active GVHD ● received a median of 9 prior regimens</td>
<td>CR (%): 38 OS (mo): NA TR (%): NR ORR (%): 50 TIR (wks): 8.1 DR (mo): NR PFS (mo): 7.8</td>
<td>PSN fatigue pyrexia nausea PSN dyspnea</td>
<td></td>
</tr>
<tr>
<td>Rothe et al, 2012</td>
<td>Pts: ● n=45 pts with ● relapsed or refractory CD30+ HL with n=34 from a NNP ● heavily pre-treated pts</td>
<td>CR (%): 22 OS (mo): NR TR (%): NR ORR (%): 60 TIR (wks): NR DR (mo): 8 PFS (mo): NR</td>
<td>PSN fatigue neutropenia diarrhea</td>
<td></td>
</tr>
<tr>
<td>Younes et al, 2012</td>
<td>Pts: ● n=102 ● relapsed or refractory CD30+ HL after auto-SCT ● received 1.8 mg/kg every 3 wks for a max of 16 cycles Study: ● Multinational, phase II, OL</td>
<td>CR (%): 34 OS (mo): NR TR (%): NR ORR (%): 75 TIR (wks): 20.5 DR (mo): 5.6 PFS (mo): NR</td>
<td>PSN fatigue neutropenia diarrhea</td>
<td></td>
</tr>
<tr>
<td>Younes et al, 2010</td>
<td>Pts: ● n= 45 pts ● relapsed or refractory CD30+ hematologic cancers (primarily HL and ALCL) ● dose of 0.1 to 3.6 mg/kg every 3 wks; pts had received median of 3 prior chemo regimens ● 73% had undergone</td>
<td>CR (%): 17 OS (mo): NR TR (%): 36 ORR (%): NR TIR (wks): 9.7 DR (mo): NR PFS (mo): NR</td>
<td>Mild to moderate</td>
<td>PSN fatigue pyrexia diarrhea nausea neutropenia PNS</td>
</tr>
</tbody>
</table>

*Note: CR = Complete Response, OS = Overall Survival, TR = Targeted Response, ORR = Overall Response Rate, TIR = Targeted Improvement Rate, DR = Duration of Remission, PFS = Progression-Free Survival, AEs = Adverse Events.*
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<td>auto-SCT</td>
<td>MTD 1.8 mg/kg</td>
<td></td>
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</tr>
<tr>
<td>Study:</td>
<td>Multicentre, phase I, OL</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>CR (%), OS (mo), TR (%), ORR (%), TtR (wks), DR (mo), PFS (mo)</td>
<td></td>
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</tr>
</tbody>
</table>

AE = adverse events; ALCL = anaplastic large cell lymphoma; alloSCT = allogeneic stem cell transplantation; auto-SCT = autologous stem-cell transplantation; CR = complete response; DE = dose-escalation; DR = duration of response; GVHD = graft versus host disease; HL = Hodgkin’s Lymphoma; mo = months; MTD = maximum tolerated dose; NPP = Named Patient Program; NA = not achieved; NR = not reported; OL = open label; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PSN = peripheral sensory neuropathy; PTCL = peripheral T-cell lymphoma; pts = patients; SALCL = systemic anaplastic large cell lymphoma; TtR = time to response; TR = tumor regression; UK = United Kingdom; wks = weeks.

a OS, TtR, DR, and PFS are presented as medians
b Results of all patients populations assessed (including those with other hematologic cancers)
c Median duration of response in the complete response population
d Median duration of response not achieved
e Overall response rate
f Actual number of patients with complete remission; not percentages
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses
No literature identified.

Randomized Controlled Trials
No literature identified.

Non-Randomized Studies


Economic Evaluations
No literature identified.
APPENDIX – FURTHER INFORMATION:

Pooled Analysis of Non-Randomized Studies


Retrospective Non-Randomized Studies


Case Series and Case Reports


Clinical Practice Guidelines

FDA Report


Review Articles


