The Cost-effectiveness of Pixantrone for Third/Fourth-line Treatment of Aggressive Non-Hodgkin's Lymphoma

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ABSTRACT

Purpose: Aggressive non-Hodgkin's lymphoma (aNHL) is associated with poor long-term survival after relapse, and treatment is limited by a lack of consensus regarding standard of care. Pixantrone was studied in a randomized trial in patients with relapsed or refractory aNHL who had failed ≥2 lines of therapy, demonstrating a significant improvement in complete or unconfirmed complete response and progression-free survival (PFS) compared with investigators' choice of single-agent therapy. The objective of this study was to assess the health economic implications of pixantrone versus current clinical practice (CCP) in the United Kingdom for patients with multiply relapsed or refractory aNHL receiving their third or fourth line of treatment.

Methods: A semi-Markov partition model based on overall survival and PFS was developed to evaluate the lifetime clinical and economic impact of treatment of multiply relapsed or refractory aNHL with pixantrone versus CCP. The empirical overall survival and PFS data from the PIX301 trial were extrapolated to a lifetime horizon. Resource use was elicited from clinical experts, and unit costs and utilities were obtained from published sources. The analysis was conducted from the perspective of the United Kingdom's National Health Service and personal social services. Outcomes evaluated were total costs, life-years, quality-adjusted life-years (QALYs), and cost per QALY gained. Deterministic and probabilistic sensitivity analyses were conducted to assess uncertainty around the results.

Findings: Pixantrone was estimated to increase life expectancy by a mean of 10.8 months per patient compared with CCP and a mean gain of 0.56 discounted QALYs. The increased health gains were associated with an increase in discounted costs of approximately £18,494 per patient. The incremental cost-effectiveness ratio of pixantrone versus CCP was £33,272 per QALY gained. Sensitivity and scenario analyses suggest that the incremental cost-effectiveness ratio was sensitive to uncertainty in the PFS and overall survival estimates and the utility values associated with each health state.

Implications: Pixantrone may be considered both clinically effective and cost-effective for patients with multiply relapsed or refractory aNHL who currently have a high level of unmet need. (*Clin Ther.* 2016;38:503–515) © 2016 The Authors. Published by Elsevier HS Journals, Inc.

Key words: cost-effectiveness, non-Hodgkin's lymphoma, pixantrone, survival analysis.

INTRODUCTION

Non-Hodgkin's lymphomas (NHL) are a heterogeneous group of diseases originating in various cells within the lymphoid system.[1] The clinical course of NHL ranges from indolent to aggressive, with diffuse large B-cell lymphoma (DLBCL) being the most common type of aggressive NHL (aNHL). DLBCL is usually diagnosed when the disease is widespread, with patients experiencing fever, fatigue, weight loss, and night sweats.[2]

Accepted for publication January 7, 2016.
http://dx.doi.org/10.1016/j.clinthera.2016.01.004
0149-2918/$ - see front matter

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First-line chemotherapy for patients with DLBCL includes rituximab with cyclophosphamide, doxorubicin, vincristine and prednisone.[1–5] However, ~50% to 60% of patients relapse within the first 2 years of treatment.[4] In as few as 10% of these patients, long-term survival with conventional salvage chemotherapies is achieved,[6] with the median survival after first relapse estimated at 4 to 6 months.[6] There is a lack of consensus with regard to standard of care, with no licensed therapies for patients with multiply relapsed or refractory NHL,[4] resulting in considerable unmet need for these patients.

Pixantrone is a novel aza-anthracenedione that was studied in a Phase III, multicenter, open-label, randomized trial in heavily pretreated patients with relapsed or refractory aNHL (ie, the PIX301 trial).[7] The efficacy and safety of pixantrone dimaleate provided at a dose of 50 mg/m^2 of active substance (or 85 mg/m^2) intravenously on days 1, 8, and 15 of a 28-day cycle, for up to 6 cycles, was examined compared with investigators' choice of single-agent therapy (vinorelbine, oxaliplatin, ifosfamide, etoposide, mitoxantrone, or gemcitabine) given at prespecified standard doses and schedules. Investigators' choice of treatments is consistent with current practice in England and Wales and is therefore referred to as current clinical practice (CCP) hereafter. Patients were followed up for 18 months after the last treatment for assessment of disease progression and survival. A significantly higher proportion of patients treated with pixantrone achieved a complete or unconfirmed complete response at the end of treatment versus those patients receiving the comparator drugs (20.0% vs 5.7%; $P = 0.021$). Progression-free survival (PFS) was significantly higher in the pixantrone group (hazard ratio, 0.60 [95% CI, 0.42–0.86]). Overall survival (OS) was not significantly longer (hazard ratio, 0.79 [95% CI, 0.53–1.18]), despite a favorable trend observed for pixantrone.[8]

As in numerous other countries, the United Kingdom's health care system requires that a new treatment be cost-effective; that is, the costs associated with a new treatment are balanced against its additional clinical benefits compared with currently used treatments. The objective of the present study was to assess the health outcomes and cost-effectiveness of pixantrone versus CCP over a lifetime for patients with multiply relapsed or refractory aNHL receiving third- or fourth-line treatment from the perspective of the UK National Health Service and personal social services.

MATERIALS AND METHODS

Model Design

A partition model was developed to estimate long-term clinical and economic outcomes for patients with multiply relapsed or refractory aNHL receiving third- or fourth-line treatment with pixantrone or CCP. CCP was assumed to comprise vinorelbine, oxaliplatin, ifosfamide, etoposide, mitoxantrone, and gemcitabine as included in the PIX301 trial.[7]

The model explored what might happen to a hypothetical cohort of patients by using a set of mutually exclusive health states: (1) stable/no progression, including progression-free patients; (2) progressive/relapsed disease, including living patients who have progressed; and (3) death. Patients can enter, remain in, or move ("transition") between health states (Figure 1). While in the stable/no progression health state, patients can stay on or discontinue initial treatment. The model cycle was set to 1 week (ie, patients can move between health states once weekly).

It was assumed that patients start in the stable/no progression health state on initial treatment. During each cycle, patients in the stable/no progression health state may remain stable and on initial treatment, or they may discontinue treatment. Alternatively, they can move to the progressive/relapsed health state or die. Patients in the progressive/relapsed health state can either remain in that state or die.

Patients were also at risk of experiencing adverse events (AEs) while on treatment in the stable/no progression state. AEs were modeled as events with cost and quality of life consequences. Treatment-emergent

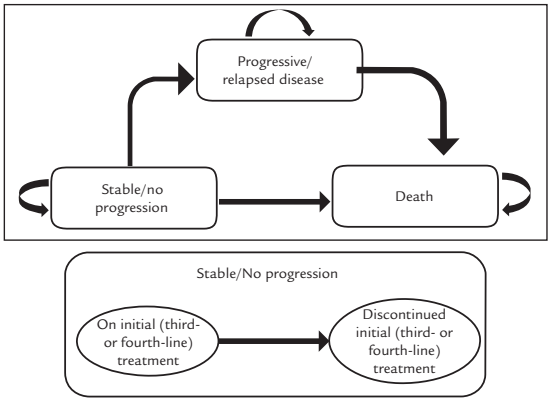

Figure 1. Model design.