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Cost-effectiveness of Ofatumumab Plus Chlorambucil in First-Line Chronic Lymphocytic Leukemia in the United Kingdom

Isobel Pearson,[1] Emma Hawe,[1] Santiago Zuluaga Sanchez,[1] Sergio Sciuto,[2*] Sorrel Wolowacz,[1] Amin Haiderali[3*]

[1] RTI Health Solutions, Manchester, United Kingdom; [2] GlaxoSmithKline, Stockley Park West, Uxbridge, Middlesex, United Kingdom; [3] GlaxoSmithKline, Collegeville, PA, United States *Previously employed by GlaxoSmithKline.

BACKGROUND

- Chronic lymphocytic leukemia (CLL) is a hematological cancer involving the propagation of a clone of mature malignant B-lymphocytes accumulated gradually in the blood, bone marrow, lymph nodes, spleen, and liver.
- Ofatumumab (O) is a fully human anti-CD20 monoclonal antibody currently indicated in the United Kingdom (UK) in combination with chlorambucil (Chl) or bendamustine in patients with CLL who have not received prior therapy and who are not eligible for fludarabine-based therapy.[1]
- The objective of this economic evaluation was to estimate whether the combination of O and ChL (OChl) is cost-effective, when compared with Chl, for the first-line treatment of CLL in patients who are not eligible for fludarabine-based therapy, from the perspective of the UK health care payer.

METHODS

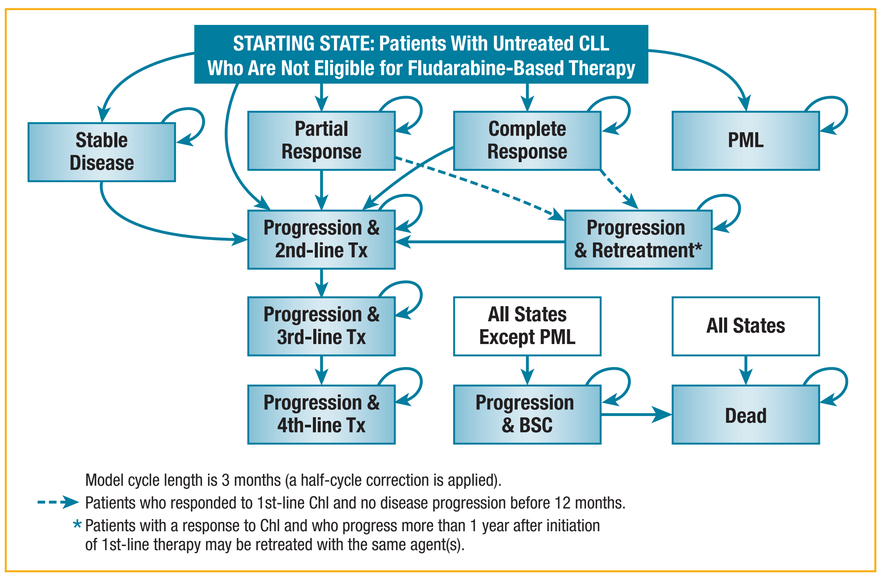
Interventions

- In the COMPLEMENT-1 trial,[2-4] Chl or OChl were administered for a minimum of three 28-day cycles and a maximum of 12 cycles or until best response, disease progression, unacceptable toxicity, or death.

Analysis Structure

- A semi-Markov decision model was developed in Microsoft Excel. The time horizon was patients' lifetime, defined as 25 years, with a cycle length of 3 months (and half-cycle correction) (Figure 1).
- Costs and health outcomes were discounted at 3.5% per annum.[5]

Figure 1. Diagrammatic Representation of the Model Structure



PML = progressive multifocal leukoencephalopathy.

Efficacy and Safety Data

- Response rates, adverse-event (AE) incidence rates, progression-free survival (PFS), and overall survival (OS) were based on the COMPLEMENT-1 trial.
  - PFS was modeled in the base case using a log-normal survival function fitted with best overall response as a covariate.
  - External long-term observations of OS for patients with CLL receiving Chl from the C9011 trial[6] were used to guide the long-term OS prediction for Chl in the model using an approach described by Hawe et al.[7]).
  - The base-case analysis assumed no continuation of any treatment effect beyond trial follow-up. Median follow-up in the COMPLEMENT-1 trial was 29 months.
- The model applied drug costs, other medical costs, and utilities for subsequent lines of therapy.
- The model incorporates costs and utility decrements associated with first-line therapy AEs and the costs associated with subsequent lines of therapy AEs.

Costs

- Key costs incorporated in the model are presented in Table 1 and Table 2.

Table 1. Drug Acquisition, Administration, and Monitoring Costs for First-Line Treatment With OChl and Chl

Cost Type	OChl	Chl	Source
Drug acquisition			
O, 100-mg vial[a]	£182.00	—	BNF, 2013[8]
Chl, 25 × 2-mg pack	£40.51	£40.51	BNF, 2013[8]
Administration			
Induction infusion in first cycle (O)	£286.60	—	Department of Health, 2013[9]
Regular infusion in subsequent cycles (O)	£255.06	—	Department of Health, 2013[9]
Oral chemotherapy dispensing (Chl)	—	£155.55	Department of Health, 2013[9]
Monitoring (per chemo cycle)[b]	£146.97	£146.97	Woods et al., 2012[10]; Department of Health, 2013[9]
Premedications (per chemo cycle)	£1.30	£1.30	Woods et al., 2012[10]; BNF, 2013[8]

[a] List price.

[b] Costs include hematologist visit, complete blood count, and biochemistry.

Table 2. Health-State Costs and Utility Values

Health State	Total Cost per 3-Month Model Cycle	Utility Weight[a]
Stable disease	£441	0.76
Partial response	£220	0.79
Complete response	£220	0.78
Progressive disease and best supportive care	£1,101	0.68[b]

[a] A baseline utility of 0.75 was applied during the first model cycle before patients transitioned to their best overall response health state.

[b] A baseline utility of 0.78 from Beusterien et al., 2010[11] was applied.

Utility Weights

- Health-state utility values (Table 2) were obtained from an analysis of the EuroQol 5 Dimensions 3-level version (EQ-5D-3L) data collected during the COMPLEMENT-1 trial.

Sensitivity Analyses

- One-way sensitivity analyses and probabilistic sensitivity analyses (PSAs) were performed.
- Various scenarios were tested in variability analysis, including different data sources for utility weights.

RESULTS

- Base-case analysis results are presented in Table 3.
- The use of intervention-specific data instead of pooled data from COMPLEMENT-1 for the proportion of patients receiving postprogression active treatment was the scenario with the largest impact on the incremental cost-effectiveness ratio (ICER). The one-way sensitivity analysis results showed that the proportions of patients advancing to subsequent lines of therapy after disease progression had the largest influence on the incremental cost per QALY gained. None of the parameters varied generated an ICER exceeding £40,000 per QALY gained.

Table 3. Base-Case Results per Patient Receiving First-Line Treatment With OChl and Chl

Model Outputs	OChl	Chl	Increment (OChl – Chl)
Costs (mean per patient, discounted)			
Cost of first-line treatment	£16,815	£2,183	£14,632
Preprogression general disease management	£1,803	£1,177	£626
Cost of retreatment and subsequent lines of treatment	£17,944	£20,762	–£2,818
Postprogression general disease management	£22,781	£24,728	–£1,948
Total cost	£59,342	£48,850	£10,492
Outcomes (mean per patient)			
Life-years (discounted)	7.18	6.85	0.33
Incremental cost per life-year gained (discounted)			£31,827

Note: Discounted refers to the costs and health outcomes discounted at 3.5% per annum.

CONCLUSIONS

- Base-case results indicated that improved overall response rates and median PFS for OChl compared with Chl translate to improved long-term health outcomes.
- The incremental cost per life-year gained in the base-case analysis, using the list price for ofatumumab, was £31,827.

REFERENCES

Please see handout for complete reference list.

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