EE277

Cost-Effectiveness of Obinutuzumab for the Treatment of Active Lupus Nephritis in the United Kingdom

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Summary

LN is one of the most severe manifestations of SLE. There is an unmet need for more treatment options to prevent the accumulation of damage and better control flares which may lead to disease progression and ultimately ESKD

Obinutuzumab in combination with ST has demonstrated a significant clinical benefit in patients with LN in terms of achieving complete renal response, reduction of proteinuria and glucocorticoid sparing, as well as reducing risk of renal flares

In this analysis, we found that obinutuzumab + ST is a highly cost-effective treatment option for adults with active LN in the UK under the NICE appraisal framework, by improving short-term response, slowing progression to ESKD and reducing long-term healthcare spending on advanced CKD

Background

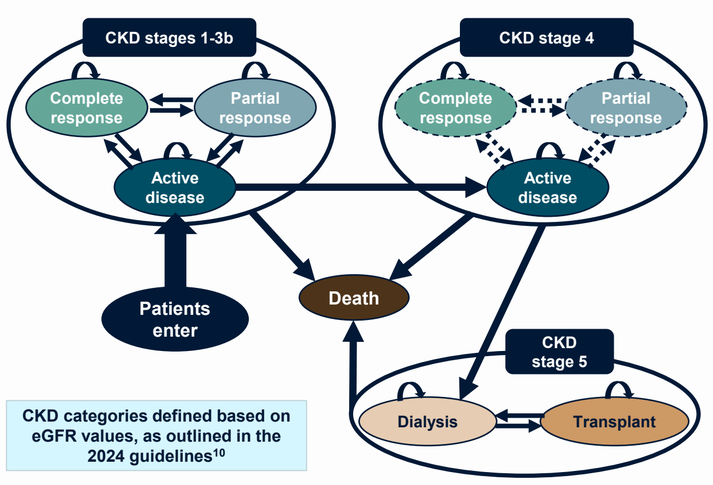
- LN is a common and severe organ manifestation of SLE for which there is no cure[1]
  - Thus, the main goal of treatment is to preserve nephrons that would be lost through inflammatory flares[2]
  - LN can lead to CKD and eventually progress to ESKD, requiring substantial use of healthcare resources including dialysis and renal transplantation[3]
- Obinutuzumab is a recombinant, humanised, glycoengineered type II anti-CD20 IgG1 monoclonal antibody that is approved for the treatment of active Class III/IV ± V LN in combination with mycophenolate mofetil[4-6]
- The REGENCY study (NCT04221477) demonstrated the efficacy of obinutuzumab in achieving rapid and deep B-cell depletion in patients with LN
  - The study met its primary endpoint, with obinutuzumab + ST (mycophenolate mofetil + corticosteroids) demonstrating a significant and clinically meaningful improvement in achievement of complete renal response at Week 76 compared with placebo + ST[7]
  - The risk of an LN flare was also lower with obinutuzumab + ST compared with placebo + ST (11.1% vs 23.5%; hazard ratio for time to flare, 0.44, *P*=0.0074; exploratory analysis)[8]
- Early treatment with obinutuzumab could preserve nephrons and delay disease progression, reducing the need to cycle through other drugs
- A cost-effectiveness model was developed for appraisal by UK health technology assessment agencies to evaluate obinutuzumab in combination with ST. The analysis attempted to translate short-term clinical trial outcomes into long-term benefits associated with delaying ESKD

Methods

Cost-effectiveness model

- To assess the cost-effectiveness of obinutuzumab in LN, a 9-state Markov model was developed (**Figure 1**) as part of the NICE appraisal for obinutuzumab in LN (TA1131)[9] which simulated patient pathways over a lifetime (70 years) from the perspective of the NHS and Personal Social Services
  - Modelling over a lifetime horizon allowed for capture of all costs and benefits associated with the treatment of LN, including those associated with progression to ESKD

Figure 1. Model structure



CKD categories defined based on eGFR values, as outlined in the 2024 guidelines[10]

- Patients entered the model in CKD stages 1-3b with active disease and transitioned between complete response, partial response, or active disease states, progressing to CKD stage 4, CKD stage 5 (dialysis or transplant) and death
- 6-monthly transition probabilities were used to capture the dynamic progression of LN over time (**Table 1**)

Clinical efficacy

- For obinutuzumab + ST versus ST alone, efficacy was derived from the REGENCY study,[7] including complete and partial renal response
- Head-to-head evidence was not available to compare obinutuzumab with other treatments; therefore, an NMA was performed for this comparison, based on published evidence from RCTs
  - The UK-relevant comparators included in this economic analysis were ST and rituximab + ST
- The voclosporin UK health technology appraisals (NICE TA882 and SMC2570) were used as sources of evidence to inform data gaps in the economic model[11,12]
  - Although voclosporin was assessed in TA1131,[9] due to its limited use in UK clinical practice it was not included in this economic analysis scenario, which focused on clinically relevant treatments used in an estimated >5% of patients in the UK
- In line with TA882, recent clinical guidelines[13] and clinical expert opinion, the model assumed that all treatments are administered for 3 years in the base case analysis

Table 1. Data sources for health state transition probabilities

Health state transition	Source
CKD1-3b active disease → CKD1-3b response (complete and partial)	• REGENCY trial[7] and NMA results
Remainder of possible transitions in the CKD1-3b states	• Individual patient transitions in REGENCY[7] • Rituximab arm: transitions assumed to be equal to those of obinutuzumab
CKD1-3b active disease → CKD4	• TA882[11] in the base case • Adjusted for impact of renal flares[8] in the analysis
Between CKD4 and CKD5 sub-health states	• Literature (Sugrue et al., 2019[14]) or TA882[11]
CKD1-3b → death	• REGENCY trial[7]
CKD4 and CKD5 → death	• Literature (Sugrue et al., 2019[14])

Due to lack of transitions data, the health states of CKD4 complete and partial response were not used in the model.

Impact of renal flares

- The NICE appraisal of obinutuzumab in LN (TA1131) acknowledged the fact that time to renal flare is linked to long-term disease progression, since flares cause damage which leads to progressive loss of kidney function[9]
- As such, the model adjusts transition probabilities using key renal flare data. Renal flare outcomes from REGENCY[8] were used to generate HRs versus key comparators. The model base case applies the HRs to adjust the risk of transitioning from CKD1-3b active disease into CKD4 to capture the impact of avoiding renal flares on long-term disease course and cost effectiveness
- The model tests the strength of the renal flare to progression to CKD4 surrogacy relationship in a threshold analysis. These scenarios vary the relative impact that avoidance of flares has on disease progression in increments of 10% from 0% (no impact) to 100% (full surrogacy)
- Renal flare HRs could also be applied to loss of response transitions (i.e., partial or complete response to active disease) in scenario analysis

Treatment effect waning

- The model applied a 3-year stopping rule across all initial therapies, after which efficacy waned linearly to ST transition probabilities
  - Obinutuzumab: 12 months of maintained effect then 12 months of waning
  - Rituximab: 6 months of maintained effect then 6 months of waning

Utilities

- HRQoL data collected in the REGENCY study were deemed to lack face validity[9] as the order of health state utilities was not reflective of utility data identified in published literature or expected by clinical experts
- Hence, utility values sourced from the NICE External Assessment Group (EAG) revised appraisal for voclosporin (TA882; **Table 2**) were utilised for all treatments in the model
- It was assumed that impacts to HRQoL from adverse reactions to treatment were already captured in health state utility values

Table 2. Summary of utility values for cost-effectiveness analysis (base case: TA882 EAG approach)

Health state	Utility value, mean (SE)	95% CI
CKD1-3b: Complete response	0.814 (0.155)	0.43, 0.99
CKD1-3b: Partial response	0.800 (0.181)	0.35, 1.00
CKD1-3b: Active disease	0.749 (0.192)	0.30, 0.99
CKD4: Complete response	0.759 (0.155)	0.40, 0.98
CKD4: Partial response	0.745 (0.149)	0.41, 0.96
CKD4: Active disease	0.694 (0.131)	0.41, 0.91
CKD5: Dialysis	0.458 (0.330)	0.00, 0.99
CKD5: Transplant	0.710 (0.270)	0.10, 1.00

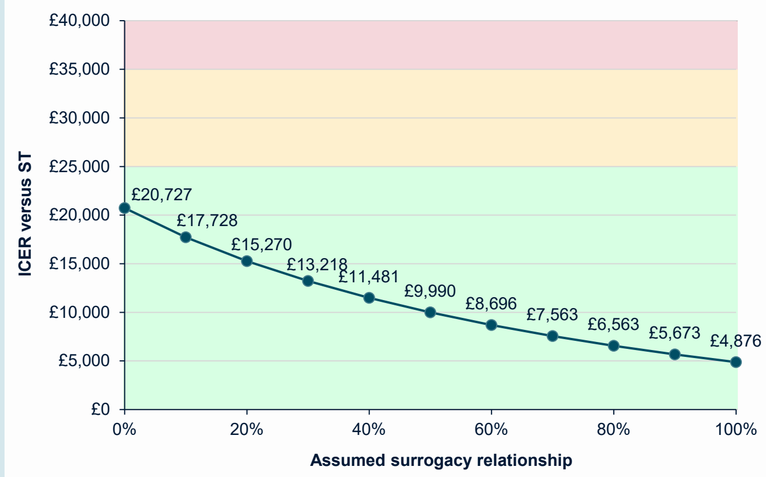
Healthcare resource use and costs

- Treatment costs were calculated based on the recommended dosing regimen for each treatment included in the model for the specified duration described in the Methods section
- Drug administration costs are accrued for the duration of treatment. Both obinutuzumab and rituximab, as well as some background corticosteroids, are administered intravenously
- Following discontinuation of initial treatment, patients go on to receive rescue or subsequent therapy for which only costs (not effects) are accounted
- Healthcare resource use was not measured in the REGENCY trial, but a systematic literature review was conducted to identify published studies reporting HRQoL data for patients with LN
- Supportive care costs in the model were considered health state–dependent and applied consistently to all treatments. In the base case, the resource use was informed by values used and validated as part of the TA882 NICE appraisal. The costs were predominantly informed by the current NHS reference costs and the Personal Social Services Research Unit report on the unit costs for health and social care[15,16]

Results

- Obinutuzumab + ST generated greater health benefits by delaying progression through CKD stages towards ESKD versus ST alone and versus rituximab + ST
- Obinutuzumab + ST resulted in an ICER of £4,876 versus ST alone (**Figure 2**) and dominated rituximab + ST at list prices when considering the impact of renal flares as a full surrogate for transition to CKD stage 4

Figure 2. Plot of incremental cost-effectiveness ratios of obinutuzumab + ST versus ST alone by assumed surrogacy relationship



- Softening this surrogacy assumption in a threshold analysis did not impact overall cost-effectiveness outcomes. Obinutuzumab + ST remained cost effective versus ST alone at a willingness-to-pay threshold of £25,000–35,000/QALY and dominated rituximab + ST at list prices
- When softening the relationship between the impact of renal flares and the transition to CKD Stage 4, assuming 50% and 25% relationship yielded an ICER of £9,990 and £14,200 versus ST alone and dominated rituximab + ST at list prices
- When eliminating the impact of renal flares completely (as preferred by the NICE committee), obinutuzumab + ST remained cost effective, with an ICER of £20,727 versus ST alone and dominant versus rituximab + ST at list price

Conclusions

- Obinutuzumab + ST provides significant health-economic benefit by improving short-term response, slowing progression to ESKD and reducing long-term healthcare spending on advanced CKD
- In the NICE appraisal (TA1131), with conservative assumptions, obinutuzumab + ST was a cost-effective treatment option for adults with active LN
- In these exploratory scenarios, when considering the clinically plausible impact of renal flares, cost-effectiveness estimates were robust to varying the surrogacy relationship. Assuming any relationship between flares and disease progression improved cost effectiveness

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Abbreviations

CD, cluster of differentiation; CI, confidence interval; CKD, chronic kidney disease; EAG, external assessment group; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio; HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio; IgG, immunoglobulin G; LN, lupus nephritis; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; NMA, network meta-analysis; QALY, quality-adjusted life-year; RCT, randomised controlled trial; SE, standard error; SLE, systemic lupus erythematosus; ST, standard therapy.

Disclosures

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