EE272

Cost-Effectiveness of Voclosporin in Combination with Mycophenolate Mofetil for Active Lupus Nephritis in Sweden

Gittfried AMV[1], Farrington E[2], Anell B[3], Norman H[4], Clamp D[2], Blaikie T[5], Ektare V[6]

[1]OPEN Health Evidence & Access, Rotterdam, The Netherlands; [2]Otsuka Pharmaceuticals Europe Ltd., Windsor, UK; [3]Otsuka Pharma Scandinavia AB, Stockholm, Sweden; [4]Quantify Research AB, Stockholm, Sweden; [5]OPEN Health Evidence & Access, London, UK; [6]OPEN Health Evidence & Access, Mumbai, India

INTRODUCTION

- Lupus nephritis (LN) is a severe renal manifestation of systemic lupus erythematosus (SLE), affecting approximately 40% to 60% of those who have SLE. Until recently, off-label immunosuppressive treatments such as mycophenolate mofetil (MMF) or cyclophosphamide were the primary treatment options. Treatment goals focus on reducing proteinuria, preserving kidney function (and prevention of CKD progression), and minimising corticosteroid exposure.
- Voclosporin (VCS) received marketing authorisation from the European Medicines Agency (EMA) on 15 September 2022 as the first licensed CNI for LN in Europe and was granted reimbursement in Sweden on 24th February 2023. In the pivotal Phase III clinical trial (AURORA 1, NCT03021499, 12 months), VCS+MMF with a low-dose steroid regimen (2.5mg/day by week 16) demonstrated a significantly improved complete renal response (CR) rate and a significant reduction in median time to urine protein/creatinine ratio (UPCR) compared to MMF and low-dose steroids alone. In the continuation study, AURORA 2 (NCT03597464; 12-36 months), patients receiving VCS+MMF had a stable estimated glomerular filtration rate (eGFR), and no unexpected safety signals.

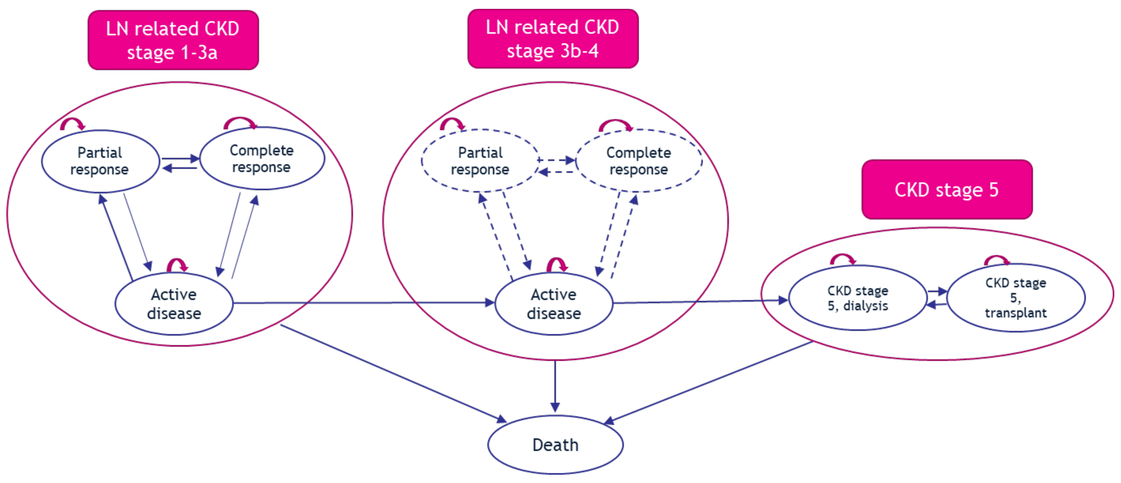
OBJECTIVES

- The objective is to assess the cost-effectiveness of VCS+MMF compared to MMF (both with low-dose steroids) in patients with active LN from a Swedish healthcare perspective.

METHODS

- A de novo Markov model with a lifetime horizon and 6-month cycle length was developed, as presented in Figure 1. Health state occupancy and quality of life inputs were estimated from individual patient data and safety data taken from the pivotal AURORA 1 trial and the continuation study AURORA 2.
- The analysis was conducted from a Swedish payer perspective as recommended by The Dental and Pharmaceutical Benefits Agency (TLV), with 3% discounting for costs and outcomes. Costs, quality-adjusted life-years (QALY), and an incremental cost-effectiveness ratio (ICER) were estimated. The willingness-to-pay (WTP) threshold was 750,000 SEK, as recommended by the TLV as the threshold for diseases of high severity. In the base case analysis, patients were assumed to be treated with VCS+MMF or MMF for 36 months, reflecting the duration of AURORA clinical trials. During this treatment period, transition probabilities for VCS+MMF and MMF were derived from the clinical trials to inform movement between health states. After 36 months, transitions for MMF were assumed to equal the average of the transition probabilities from the last two periods (months 24-30 and months 30-36). VCS+MMF was conservatively assumed to have the same transitions as MMF due to a lack of data beyond 36 months.
- Deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) of 1,000 iterations were used to assess the robustness of results. Upper and lower bounds of variables tested in the DSA were determined based on increasing/decreasing the base case value by the standard error, or 20% of the base case value when not reported.
- The following scenarios were tested:
  - Treatment duration at 18, 48, and 72 months (only costs updated for latter two due to a lack of data beyond 36 months)
  - Long-term transitions (after 36 months) in CKD1-3a updated for VCS+MMF using the midpoint between the weighted transitions for VCS+MMF and MMF
  - Literature based transition probabilities and utilities were tested in place of AURORA trial-based values

Figure 1. Model structure diagram



Note: The model includes functionality for patients with AD CKD 3b-4 to transition to PR or CR states; however, the base case analysis does not use CKD 3b-4 response states as no patients transitioned to CKD 3b-4 during the 36-month study period and lack of alternative data.

Abbreviations. CKD: chronic kidney disease; LN: lupus nephritis. CR: complete renal response; PR: partial renal response.

RESULTS

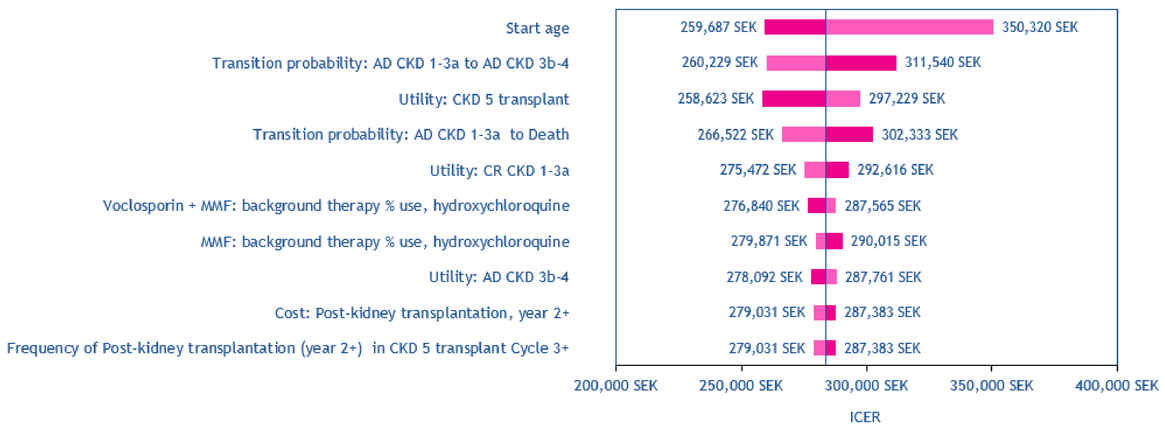
Base case

- In the base case analysis, VCS+MMF resulted in 0.676 additional QALYs and additional costs of 191,800 SEK, with an ICER of 283,611 SEK/QALY compared to MMF.

Sensitivity analyses

- The DSA (Figure 2) indicated that for all one-way sensitivity analyses, VCS+MMF remained cost-effective versus MMF, with baseline age, the transition between active disease in CKD 1-3a and active disease in CKD 3b-4, and the utility of the CKD 5 transplant health state having the highest impact on the ICER. Similarly, the PSA outcomes (Figure 3) show that from a WTP-threshold of approximately 270,000 SEK/QALY, VCS+MMF is cost-effective compared to MMF.

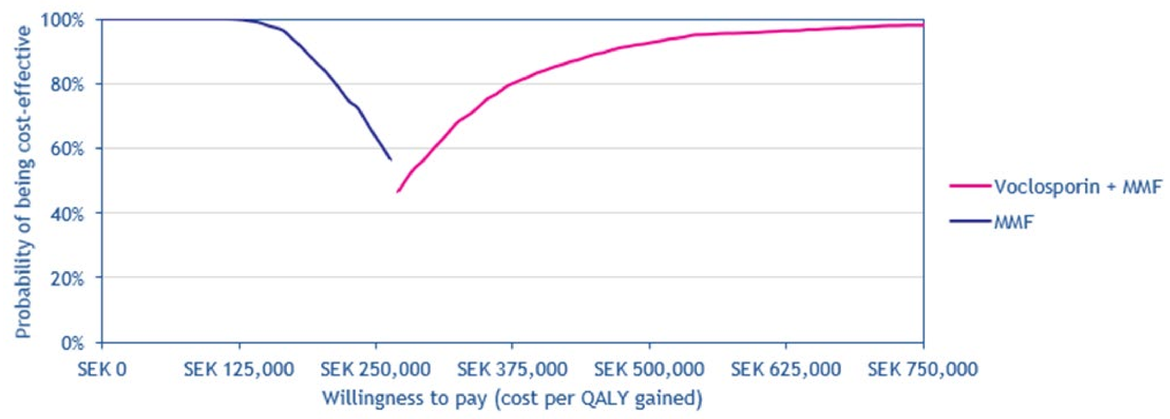
Figure 2. Tornado diagram of DSA results on the ICER



Abbreviations. AD: active disease; CKD: chronic kidney disease; DSA: deterministic sensitivity analysis; ICER: incremental cost-effectiveness ratio; MMF: mycophenolate mofetil.

RESULTS

Figure 3. Cost-effectiveness acceptability frontier



Abbreviations. MMF: mycophenolate mofetil; QALY: quality-adjusted life year.

Scenario analysis

- Table 1 presents the result for scenario analyses. In the scenario analyses, adjusting the treatment duration and the long-term treatment effect had the highest impact on the ICER.

Table 1. Scenario analyses result

Scenarios	Costs (SEK)	QALYs (Years)	ICER (SEK/QALYs)
Base case	1,263,982	14.706	283,611
Treatment duration costings			
18 months	1,083,243	13.767	269,869
48 months	1,309,455	14.706	349,546
72 months	1,381,115	14.706	454,257
Long-term transition probabilities			
Weighted transition of MMF and VCS+MMF	1,212,315	15.204	119,374
Transition probabilities			
Liu et al., 2021 – overall population* (1.53%, 0.52%, 2.13%)†	1,231,061	17.203	414,553
Liu et al., 2021 – mild CKD at baseline & moderate albuminuria* (2.86%, 0.74%, 3.64%)†	1,259,914	15.917	329,680
Liu et al., 2021 – mild CKD at baseline & severe albuminuria* (6.79%, 0.86%, 8.60%)†	1,382,993	13.769	245,168
Utility source			
Bexelius et al., 2013; Mohara et al., 2014 (0.800, 0.710, 0.620)††	1,263,982	13.546	278,389

*Liu et al., 2021 overall population is not stratified by albuminuria. Populations with moderate or severe albuminuria in Liu et al., 2021 match more closely to the patient population enrolled into the AURORA clinical trial

† Values in brackets are transition probabilities from AD CKD 1-3a to AD CKD 3b-4, from AD CKD 1-3a to Death, and from AD CKD 3b-4 to Dialysis, respectively

†† Values in brackets are utilities in CR CKD 1-3a, PR CKD 1-3a, and AD CKD 1-3a, respectively

Note: Liu et al., 2021 defines moderate albuminuria as protein-to-creatinine ratio 150-500mg/g and severe albuminuria as protein-to-creatinine ratio >500mg/g. Patient population enrolled into the AURORA clinical trial has mean baseline UPCR as 4.14 mg/mg.

Abbreviations. AD: active disease; CKD: chronic kidney disease; CR: complete renal response; ICER: incremental cost-effectiveness ratio; MMF: mycophenolate mofetil; QALY: quality-adjusted life year; PR: partial renal response; VCS: voclosporin.

CONCLUSIONS

- Based on a willingness-to-pay threshold of 750,000 SEK for diseases of high severity, VCS+MMF is a cost-effective treatment compared to MMF for adults with active lupus nephritis in Sweden. Although uncertainty exists in the available data to support transitions in the long-term (after 36 months) and between CKD stages included in the model, extensive sensitivity and scenario analysis indicate that results are robust.

REFERENCES

1. Attema et al., PharmacoEconomics, 2018, 36(7), 745-758.
2. Bexelius et al., Lupus, 2013, 22(8), 793-801.
3. Liu et al., JAMA Network Open, 2021, 4(6), e2112828.
4. Mohara et al., Rheumatology, 2014, 53(1), 138-144.
5. Rovin, et al., Lancet, 2021, 397(10289), 2070-2080.
6. Aurinia Pharmaceuticals Inc. (2022). Clinical Trial Registration NCT03597464. https://clinicaltrials.gov/study/NCT03597464

DISCLOSURES

AG, TB and VE are employees of OPEN Health Evidence & Access, which received consultancy fees from Otsuka Pharmaceuticals Europe Ltd. EF and DC are employees of Otsuka Pharmaceuticals Europe Ltd. and AB is an employee of Otsuka Pharma Scandinavia AB. HN is an employee of Quantify Research AB, which received consultancy fees from Otsuka Pharma Scandinavia AB.

Medical Writing Support: the authors thank Jessica Shi of OPEN Health for writing and design support, which was sponsored by Otsuka Pharmaceuticals Europe Ltd. in accordance with Good Publication Practice guidelines.

Presented at: ISPOR Europe 2023, Copenhagen, Denmark, 12-15 November 2023