Personalized Spacing of Eculizumab Infusions Based on Therapeutic Drug Monitoring compared with continuation of the usual dosing regimen in Atypical Hemolytic-Uremic Syndrome Requiring Long-term Treatment: a trial-based cost-utility analysis from ESPACECU.

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Abstract:

Introduction: Atypical Hemolytic-Uremic Syndrome is a rare disease. Since 2011, eculizumab is an anti-C5 monoclonal antibody approved for aHUS. It is administered by intravenous infusions in hospital. The maintenance phase dosing regimen is identical for all adult patients (1200 mg every 14 days). Several studies showed high inter-individual kinetics variability, with very high trough concentrations in some patients. Therefore eculizumab administration intervals could be extended in overexposed patients, based on therapeutic drug monitoring (TDM). As eculizumab is an expensive drug, this personalization strategy is expected to result in substantial cost savings compared to maintaining the usual dosing regimen. The impact on patients' quality of life is to be determined. As primary objective, we assessed the cost-effectiveness of this strategy using a trial-based cost-utility analysis

Methods: EspacECU study was designed as a multicenter two-arm 2:1 randomized controlled trial. Thirty-eight patients in remission who require life-long treatment, with no possibility of discontinuation due to their genetic characteristics or history of kidney transplantation were enrolled and analyzed. In the experimental group, the spacing of eculizumab infusions was personalized based on a bayesian pharmacokinetic model. The control group continued the prestudy administration scheme without personalization. Differences in costs and QALYs were estimated over an 18-month period from the French Health Insurance. Structural and parametric uncertainty was explored.

Results: Based on frequentist adjusted models, the innovative strategy resulted in a statistically significant reduction in mean cost per patient (–€40 573). No significant difference in QALYs was shown. Eculizumab price was the main cost driver.

Conclusion: Personalized spacing of eculizumab infusions based on TDM can be considered as a cost-effectiveness strategy, thanks to the savings achieved without any demonstrated loss of quality of life. The widespread adoption of this strategy in clinical practice promises substantial savings for the National Health Insurance, which cannot be overlooked in times of chronic deficit.

Ethics and dissemination: EspacECU study is registered at Clinicaltrials. Gov. It was approved by a French Committee for the Protection of Persons (Sud-Méditerranée II) and the French drug regulatory authority.

Trial registration number NCT04859608.
https://clinicaltrials.gov/ct2/show/NCT04859608

Key words:

atypical hemolytic uremic syndrome, cost-utility analysis, eculizumab, QALY, therapeutic drug monitoring, dose tapering, pharmacokinetics