Cost-Effectiveness Model Conceptualisation in Chronic Graft-Versus-Host Disease

MSR149

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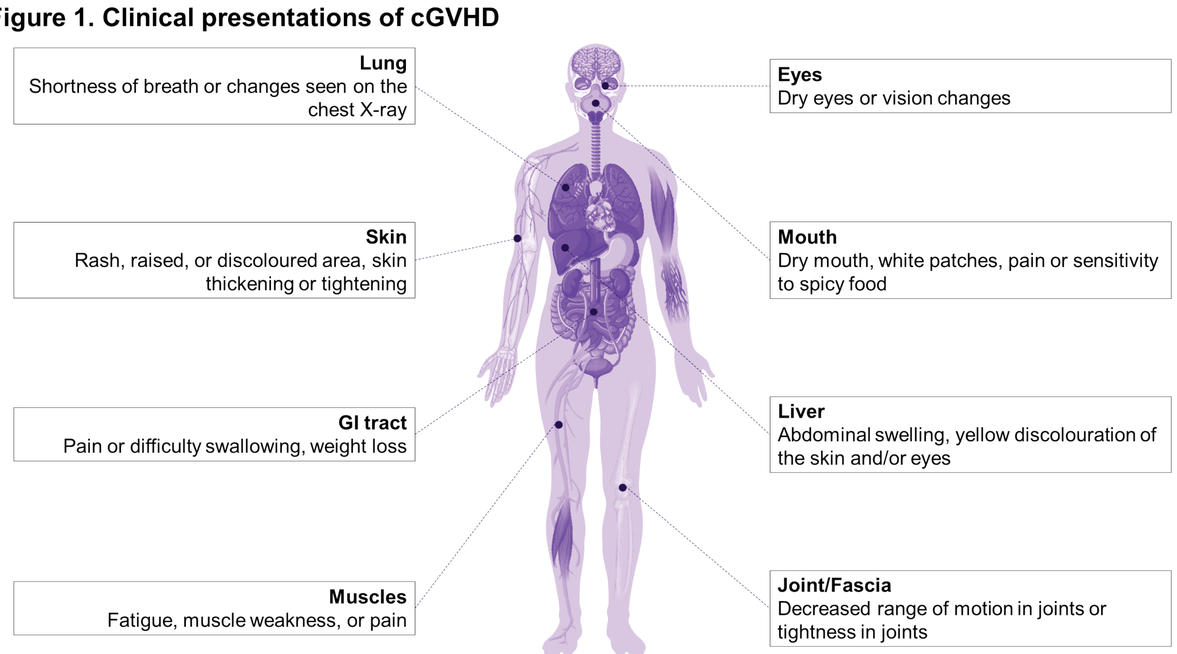
BACKGROUND

- Graft-versus-host disease (GVHD) is an immune-mediated condition resulting from the complex interaction of donor lymphocytes against the normal cells of the recipient.[1]
- GVHD both in acute and chronic forms is a serious complication following an allogeneic transplant, limiting its success.[2,3]
- While acute GVHD primarily affects the skin, gastrointestinal tract, and liver, chronic GVHD (cGVHD) can manifest in multiple organs, including the skin, mouth and eyes, gastrointestinal tract, liver, musculoskeletal tissue, and lungs. **Figure 1** shows the various clinical manifestations of cGVHD.[2,3]
- There are very few cost-effectiveness models evaluating treatments for cGVHD, and those are simple models based on published literature and assumptions.[4,5]
- Failure-free survival (FFS) is recognised as a clinically relevant endpoint in cGvHD and captures the time spent on a line of therapy, with failure resulting from switching to a new treatment, recurrent malignancy, or death.[6]
- A model examining the effect of treatments on response needs to consider response across multiple organs, each with multiple severity levels of impact. The complexity of this, and the lack of data to inform this, warrants a pragmatic approach.

Figure 1. Clinical presentations of cGVHD



cGVHD, chronic graft-versus-host disease; GI, gastrointestinal

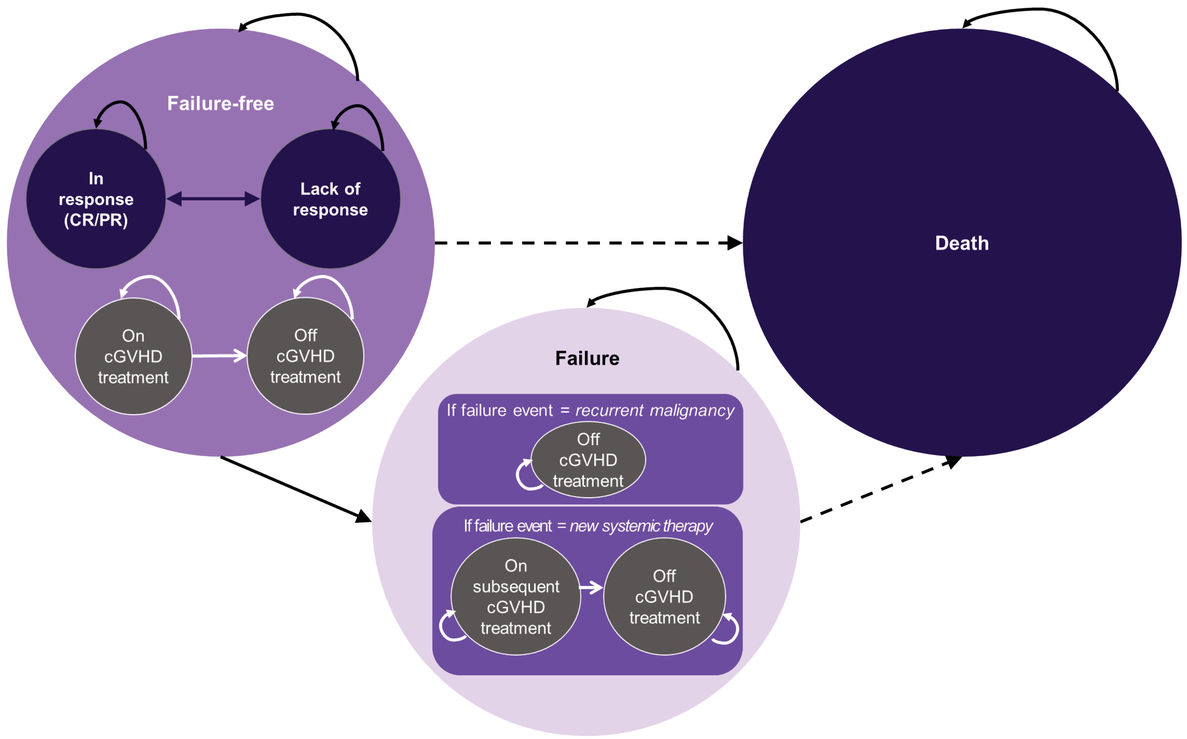
OBJECTIVES

- The objective of the study was to develop an economic analysis model that utilises FFS data to estimate the mean costs and benefits of cGVHD treatments.

METHODS

- A partitioned survival (or area under the curve) model with a 4-week cycle was used, which reflects the progressive nature of cGVHD and a potential relapse to underlying malignancies.
- This model, developed in Microsoft Excel®, estimates the clinical and economic outcomes of cGVHD treatments over a lifetime horizon and comprises three health states: failure-free (FF), failure, and death.
- This model uses FFS as the central endpoint.
  - Patients enter the model in the FF state and may transition to the failure state after experiencing a recurrence of their malignancy or the initiation of a new cGVHD systemic therapy (different costs and utilities are assigned to each cause of failure). Patients may transition to the death state either from the FF or the failure state **(Figure 2)**.

Figure 2. Model structure



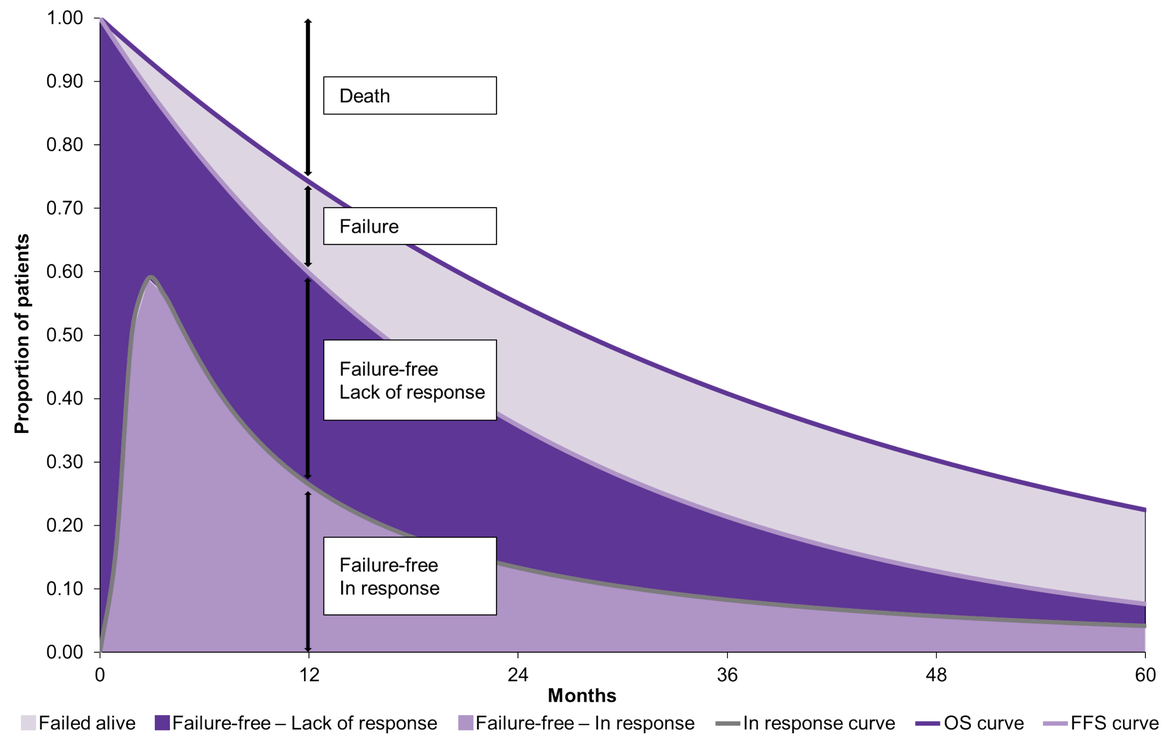
cGVHD, chronic graft-versus-host disease; CR, complete response; PR, partial response

- The transitions between these three health states are informed by FFS and overall survival (OS) curves for each treatment.
- The model offers the flexibility to account or not account for response status (complete response [CR], partial response [PR], or a lack of response [LR]) within the FF state using time to response (TTR) and duration of response (DOR) data.
- Patient's quality of life associated with the treatment and disease outcomes was captured by applying utility values to the FF and failure states.

RESULTS

- An illustration of the partitioned survival of patients in the three health states (FF, failure, and death) and with different response levels at each point in time is shown in **Figure 3**.

Figure 3. Partitioned survival model



Note: Lack of response includes stable disease. FFS, failure-free survival; OS, overall survival.

- The area under the OS curve determines the proportion of patients who are still alive over time, while the area under the FFS curve determines the proportion of patients in the FF state.
- The proportion of patients in the failure state can be calculated as the area between the FFS and OS curves at a given time point.
- An 'In response' curve was created from the TTR and DOR curves and used to separate patients who were 'In response' (i.e., CR or PR) from those with LR within the FF state.
- The model was populated with data from pooled analyses of the ROCKstar and Phase 2a clinical trials for belumosudil[6,7] and the REACH[3] trial[8] for best available therapy (BAT) for cGVHD and was used to estimate lifetime clinical outcomes.
- The mean utility values were calculated based on Patient-Reported Outcomes Measurement Information System (PROMIS) data from the ROCKstar trial mapped to EQ-5D for the FF state. Utility values from published literature were used for the failure state.
- The life years (LYs) and quality-adjusted life years (QALYs) gained (discounted at 3.5% per annum) were 6.77 and 3.58 for belumosudil versus 5.52 and 2.10 with BAT, respectively (**Table 1**). The LYs and QALYs in the FF state were higher for belumosudil compared with BAT.

Table 1. Comparison of health outcomes per patient between belumosudil and BAT treatment cohorts

Outcome	Belumosudil	BAT†	Incremental outcome (Belumosudil–BAT)
Total Lys	6.77	5.52	1.25
Failure-free	3.99	1.02	2.97
In response	2.15	0.78	1.37
Lack of response	1.84	0.23	1.6
Failure	2.78	4.51	−1.73
New cGVHD systemic therapy	2.4	4.25	−1.85
Recurrent malignancy	0.37	0.25	0.12
Total QALYs*	3.58	2.1	1.48
Failure-free	2.88	0.76	2.12
In response	1.58	0.59	1
Lack of response	1.29	0.17	1.12
Failure	1.27	2.05	−0.78
New cGVHD systemic therapy	1.1	1.93	−0.83
Recurrent malignancy	0.17	0.11	0.06

*The total QALYs presented here do not match the sum of the QALYs in the different health states in the table, as some other QALY categories are not displayed (decrement due to AEs; decrement associated with IV infusion; decrement related to caregivers' quality of life). †BAT consisted of extracorporeal photopheresis, mycophenolate mofetil, ibrutinib, low-dose methotrexate, imatinib, sirolimus, rituximab, everolimus and infliximab.
AE, adverse event; BAT, best available treatment; cGVHD, chronic graft-versus-host disease; IV, intravenous; LYs, life years; QALYs, quality-adjusted life years

STRENGTHS

- One of the primary strengths of the partitioned survival approach is its ability to capture pivotal clinical outcomes, such as FFS and OS, making it a valuable tool for analysing patient outcomes.
- This model captures the expected clinically important differences in costs and outcomes among patients in FF and failure states.
  - Within the FF state, patients can be segregated by response level, allowing estimations of differences in costs and utilities across the response levels.
  - Within the failure state, patients can be segregated by the cause of failure, allowing estimation of costs and utilities across the sub-states.

CONCLUSIONS

- This model, focused on FFS outcomes, provides an innovative and relevant perspective for cost-effectiveness analysis.
- It not only captures the intricate patient journey but also sheds light on the tangible value of cGVHD treatments.

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CONFLICTS OF INTEREST
EL, AJOA, RH, LS, and **CN** are employees of and stockholders in Sanofi. **TK, IH, GS, TP,** and **BD** are employees of Evidera, which received financial support from Sanofi for the development of this study.
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