Cost Effectiveness of Treatments for Peripheral T-Cell Lymphoma

James W. Gilmore[1], Jesse D. Ortendahl[2], Ayanna M. Anene[2], Tanya G.K. Bentley[2], Michael McGuire[3]

[1]Georgia Cancer Specialists; [2]Partnership for Health Analytic Research; [3]Celgene Corporation

INTRODUCTION & OBJECTIVE

- Peripheral T-Cell Lymphoma (PTCL) is a rare yet aggressive form of non-Hodgkin Lymphoma.
- Survival varies by histologic subtype, with the most common types reporting 5-year survival rates of 32%[1].
- Initial treatment typically consists of combination chemotherapy regimens; however, patients often fail to respond or quickly relapse.
- For relapsed/refractory PTCL patients, three targeted therapies are FDA-approved and used in clinical practice:
  - Romidepsin (Istodax) 14mg/m^2 on days 1,8 and 15 of a 28-day cycle
  - Pralatrexate (Folotyn) 30mg/m^2 once weekly for 6 weeks of a 7-week cycle
  - Belinostat (Beleodaq) 1,000mg/m^2 on days 1-5 of a 21-day cycle
- These therapies gained approval based on their efficacy in single arm clinical trials, and there have been no pairwise assessments of these treatments in trials.
- In addition, information is lacking regarding the economic impact of these treatment options in relapsed/refractory PTCL patients for guiding treatment decision making.
- This analysis used economic modeling to evaluate the cost effectiveness of romidepsin, pralatrexate, and belinostat in treating relapsed/refractory PTCL patients.

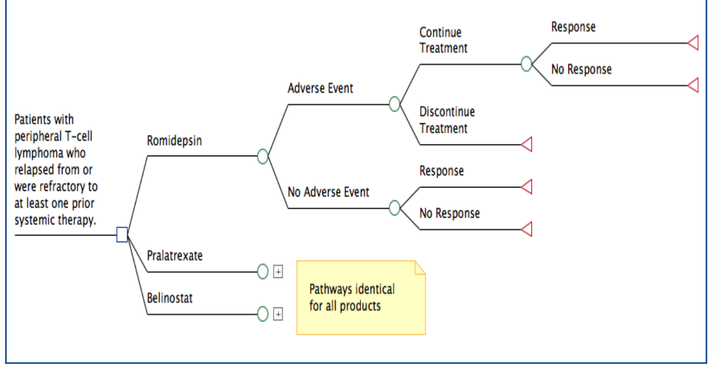
METHODS

Model Overview:

- Type: Deterministic cohort model programmed in TreeAge Pro 2012
- Population: Relapsed/refractory PTCL patients
- Perspective: US Payer
- Currency: 2015 $US
- Time Horizon: 18-weeks or until treatment discontinuation
- Model Inputs: Drug acquisition and administration costs, adverse event (AE) rates and costs, patient response rate and duration
- Outcome Measures: Cost per patient, average duration of response (among responders and for the full cohort of treated patients), $/additional month of response

Model Structure:

Figure 1. Model Schematic



- Relapsed/refractory PTCL patients enter the model and initiate one of three treatments.
- Patients remain in the model and accrue costs until they discontinue treatment due to: lack of treatment response; disease progression; or discontinuation due to AEs.
- Total costs and clinical outcomes (i.e., response duration) for each treatment pathway are calculated as per-patient averages based on the proportions of patients following each pathway.

Model Inputs

Model inputs related to clinical response were collected from the pivotal, single arm Phase 2 clinical trials for each product.

Table 1. Patient Characteristics from Clinical Trials

	Romidepsin (n=130)[2]	Pralatrexate (n=111)[3]	Belinostat (n=120)[4]
% Male	68%	68%	52%
Median Age	61	58	64
ECOG			
0-1	86%	n/a	78%
2	13%	n/a	22%
Subtype			
PTCL NOS	53%	53%	64%
ALCL	16%	15%	13%
AITL	21%	12%	18%
Prior Transplant	16%	16%	25%

- No adjustments were made for differences in trials' populations due to the single arm trial design for all products. However, the patient populations had a similar proportion of patients with each subtype (Table 1).

Table 2. Clinical Parameters

	Romidepsin[2]	Pralatrexate[3]	Belinostat[4]
Patients Responding (%)	25%	29%	26%
Complete	15%	11%	11%
Partial	11%	18%	15%
Stable Disease	18%	19%	15%
Duration of Response (months)	28.0	10.1	13.6

- Response rates were similar across products and assessed using the NCI-IWG criteria. Duration of response among responders was greater for patients treated with romidepsin (Table 2).
- Product acquisition and administration costs were estimated using pricing databases, dosing schedules from product prescribing information, and utilization from the respective clinical trials (Table 3).

Table 3. Product Costs

	Product Costs per Treatment Cycle		Average Treatment Cycles per Patient[2,3,4]	Treatment Costs Per Patient in Trial	Cost Per Month of Treatment
	Acquisition[5]	Administration[6]			
Romidepsin	$26,345	$2,531	4.5	$129,939	$31,969
Pralatrexate	$78,018	$2,244	2.6	$208,681	$50,778
Belinostat	$31,950	$2,523	6.0	$206,837	$50,889

METHODS (continued)

- The impact of treatment toxicity was incorporated into the model through inclusion of select grade 3+ AEs. Events were included if they occurred in >10% of patients in any of the trials.
- Costs associated with each AE were estimated based on published literature[7-12] (Table 4).

Table 4. Adverse Event Rates and Costs

	Thrombocytopenia	Mucositis	Neutropenia	Anemia	Leukopenia	Upper Respiratory Infection+	Pneumonia	Sepsis
Product-specific Event Rates								
Romidepsin[2]	24%	0%	20%	11%	6%	8%	6%	5%
Pralatrexate[3]	33%	22%	22%	18%	8%	1%	0%	5%
Belinostat[4]	7%	0%	6%	11%	0%	0%	5%	0%
Event Costs[5-12]	$1,383	$7,360	$8,779	$26,880	$13,622	$0.36	$17,420	$30,307

+Assumed no inpatient hospitalization was required for infection and treated with generic antibiotics

ANALYSES CONDUCTED

- In the base case analysis, average costs and duration of response for each therapy were estimated. Model outcomes were used to calculate incremental cost effectiveness ratios.
- One-way sensitivity analyses were conducted, in which pairwise comparisons were made between romidepsin and each alternative therapy when varying parameters individually +/- 20% of the base case value.
- Probabilistic sensitivity analyses were conducted in which all parameters were varied simultaneously across 1,000 model iterations.

BASE CASE RESULTS

Base Case Results (Table 5):

- The model showed that patients treated with romidepsin had the lowest costs ($138,362), compared with costs for belinostat and pralatrexate of $211,289 and $220,132, respectively. The average duration of response, among responders, was highest for romidepsin (28.0 months), vs. belinostat (13.6 months) and pralatrexate (10.1 months).
- These model outputs led to the conclusion that romidepsin was the dominant treatment option compared to both belinostat and pralatrexate (i.e., provided greater clinical benefit at a lower cost) after adjusting for differences in efficacy and safety.
- When considering all initially treated patients, those on romidepsin had an average response of 7.1 months, compared with 3.5 months and 2.9 months for those treated with belinostat and pralatrexate, respectively. The finding that romidepsin was the dominant treatment is unchanged from the base case.
- Total cost differences between treatment pathways is driven primarily by product acquisition costs.

Table 5. Base Case Results Among Patients Responding

Product	Total Costs	Δ Costs	Total DOR	Δ DOR	ICER
Romidepsin	$138,362	-	28	-	-
Belinostat	$211,289	$72,927	13.6	-14.4	Dominated
Pralatrexate	$220,132	$8,843	10.1	-3.5	Dominated

Δ, incremental; DOR, duration of response; ICER, incremental cost-effectiveness ratio.

SENSITIVITY ANALYSIS RESULTS

- In one-way sensitivity analyses:
  - Results were most sensitive to response durations, product acquisition costs, and product administration costs.
  - As in the base case, romidepsin remained the least expensive strategy with the greatest clinical benefit.
- In probabilistic sensitivity analyses:
  - Romidepsin had a consistently longer response duration than both pralatrexate and belinostat.
  - Romidepsin was cost-saving compared with pralatrexate in 99.6% of iterations, and in 98.5% when compared with belinostat.

CONCLUSIONS

- Results suggest that treating PTCL patients with romidepsin may enhance clinical benefit by extending duration of response at a lower cost compared to alternatives.
- Data limitations prevented adjustment of differences in clinical trial populations, consideration of a longer time-horizon, inclusion of subsequent lines of therapy, or comparison of survival. Future analyses should also take into account real-world treatment patterns, efficacy, and costs associated with PTCL treatment options.
- Clinicians, payers, and policy makers should consider this finding of romidepsin demonstrating greater clinical benefit at a reduced cost as one aspect in making healthcare resource allocation decisions.

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CORRESPONDENCE

Michael McGuire– mmcguire@celgene.com

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