soho2023
ELEVENTH ANNUAL MEETING

PHARMACOKINETICS AND SAFETY OF BENDAMUSTINE IN THE BEABOVP REGIMEN FOR THE TREATMENT OF PEDIATRIC PATIENTS WITH HODGKIN LYMPHOMA

K. Purvis[1], H. Swanson[2], K. Kulldeep Niloy[2,3], Y. Zhou[4], J. Panetta[2], K. Crews[2], J. Flerlage[5]

1. University of Tennessee Health Sciences Center, Memphis, TN USA
2. Department of Pharmacy and Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, TN, USA
3. Department of Pharmaceutical Sciences, University of Tennessee Health Science Center, Memphis, TN, 38163, USA
4. Department of Biostatistics, University of Tennessee Health Science Center, Memphis, TN, 38163, USA
5. Department of Oncology, St. Jude Children's Research Hospital, The University of Tennessee Health Science Center, 262 Danny Thomas Pl, Mailstop 260, Memphis, TN 38105, USA

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INTRODUCTION

The Stanford V chemotherapy regimen has been used to treat Hodgkin Lymphoma (HL) patients since 2002 with excellent cure rates; however, mechlorethamine is no longer available. Bendamustine is being substituted for mechlorethamine in combination therapy in a frontline trial for low- and intermediate-risk pediatric HL patients, forming a new backbone of BEABOVP (bendamustine, etoposide, doxorubicin, bleomycin, vincristine, vinblastine, prednisone).

AIM

To evaluate the pharmacokinetics and tolerability of bendamustine in BEABOVP and determine factors that may explain any observed variability.

METHOD

- Low- and intermediate-risk classical HL patients receiving BEABOVP were eligible
- **Bendamustine** was substituted for **mechlorethamine** in the **Stanford V backbone**
- Bendamustine plasma concentrations were measured in 118 samples from **20 pediatric patients**
- A pharmacokinetic model was fit to the data by using nonlinear mixed-effects modeling.

RESULTS

- Patients ranged in age from 4.9 to 21.4 years
- There was a trend **toward decreasing clearance** with **increasing age** (p=0.074)
- **Age** explained 23% of the **inter-individual variability** in clearance.
- Median (range) AUC was 12,415 (8,539, 18,642) µg hr/L
- Median (range) maximum bendamustine concentration was 11,708 (8,034, 15,741) µg/L
- Regimen was **well tolerated** with no grade 3 toxicities resulting in treatment delays of more than 7 days.

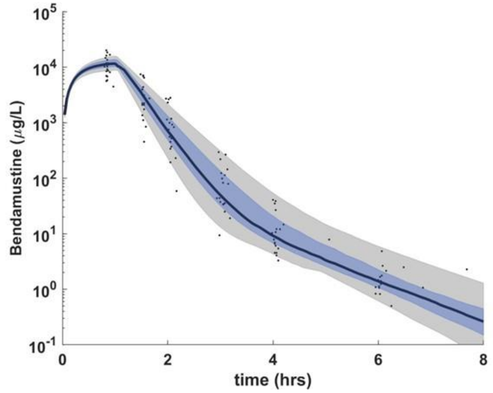


Figure 1: Bendamustine concentration vs time. Black dots: measured Bendamustine; Black curve: median estimated concentration; Blue shaded region: 25th-75th percentile of estimated concentrations; Grey shaded region 5th-95th percentile of estimated concentrations.

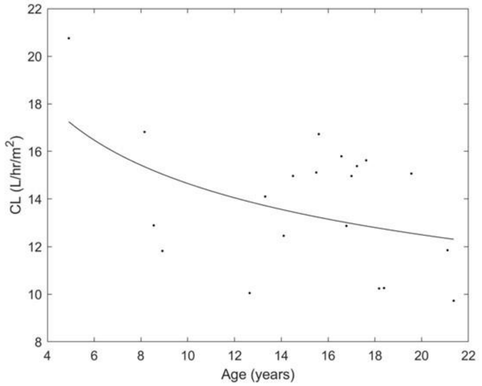


Figure 2: Bendamustine CL vs age.

CONCLUSIONS

- A single-day dose of 180 mg/m^2 of bendamustine every 28 days was safe and **well tolerated** in pediatric patients with HL receiving BEABOVP therapy.
- Age accounted for 23% of inter-individual variability observed in bendamustine clearance.
- A new standard of care should be considered to allow for single-day dosing of bendamustine instead of splitting the dose over two days

REFERENCES

1 **Jeha S et al**. Phase 1 study of bendamustine in combination with clofarabine, etoposide, and dexamethasone in pediatric patients with relapsed or refractory hematologic malignancies. *Cancer 2021; 127(12);: 2074-2082.*

2 **Purvis K et al.** Pharmacokinetics and safety of bendamustine in the BEABOVP regimen for the treatment of pediatric patients with Hodgkin lymphoma. *Cancer Chemotherapy and Pharmacology 2023; 92(1);: 1-6*

ACKNOWLEDGEMENTS

This study was supported in part by the NIH Cancer Center Support Grant CA21765 and the American Lebanese Syrian Associated Charities (ALSAC). Jamie Flerlage is supported by the Lymphoma Research Foundation.

CONTACT INFORMATION

Jamie Flerlage, MD, MS; Research Associate Department of Oncology; St Jude Children's Research Hospital; 262 Danny Thomas Pl, Mailstop 260, Memphis, TN 38105; jamie.flerlage@stjude.org; phone: +1-901-595-0392; fax: +1-901-521-9005