Budget Impact Analysis of *TPMT* and *NUDT15* Pharmacogenomic Testing for 6-Mercaptopurine in Pediatric Acute Lymphocytic Leukemia Patients

Beverly Fuerte, Mia Burgos, Vyvy Cao, Jenny Nguyen, PharmD, Simran Maggo, PhD, Deepa Bhojwani, MD, Teresa Rushing, PharmD, Cynthia L. Gong, PharmD, PhD

INTRODUCTION

- **Pharmacogenomic (PGx) testing** identifies genetic variations affecting drug metabolism, which is crucial for optimizing dosing and minimizing adverse effects[1]
- **6-mercaptopurine (6-MP)** is a core backbone in the treatment of **acute lymphocytic leukemia (ALL)**[1], with ***TPMT* and *NUDT15* genetic variations** significantly impacting 6-MP metabolism[2,3]

METHODS

Literature search utilizing the PubMed and Cochrane databases to identify papers published between January 1, 2000 and August 1, 2023. Relevant articles discussed:
- 6-mercaptopurine administration
- Pediatric ALL (children aged 0-18 years old)
- *TPMT* or *NUDT15* genetic testing
- Outcomes of cost-effectiveness

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Construction of **hypothetical model population** of 1000 pediatric patients with ALL using epidemiology data and CPIC biogeographical data of *TPMT* and *NUDT15* genotype frequencies.[4,5]

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Building of **Markov model** to simulate the process for initiation of 6-MP in maintenance phase of ALL chemotherapy regimen dosing based on preemptive PGx testing or no testing and degree of myelosuppression.[6]

RESULTS

- In a hypothetical cohort of 1,000 pediatric patients with ALL, a total of 157 In the base case, we found an **overall healthcare cost savings of $26,026** for inpatient and outpatient management of myelosuppression in ALL patients with preemptive PGx testing.

DISCUSSION

- Pre-emptive PGx testing yields cost-savings by **reducing moderate and severe myelosuppression episodes**
- Cost-savings **primarily influenced by the cost of outpatient management of moderate myelosuppression**
- **Actual PGx test results had a marginal impact on cost-savings**
- Integration into routine clinical practice can be **challenging due to resource constraints, time limitations, and knowledge level of healthcare providers**[7,8]
- **Lack of evidence** of clinical benefits and cost-effectiveness can lead to **inadequate reimbursement** from payers and a **decrease in patient accessibility**[9]

Preemptive pharmacogenetics testing is associated with cost savings of $26,026 in pediatric ALL patients

due to reduced myelosuppression costs

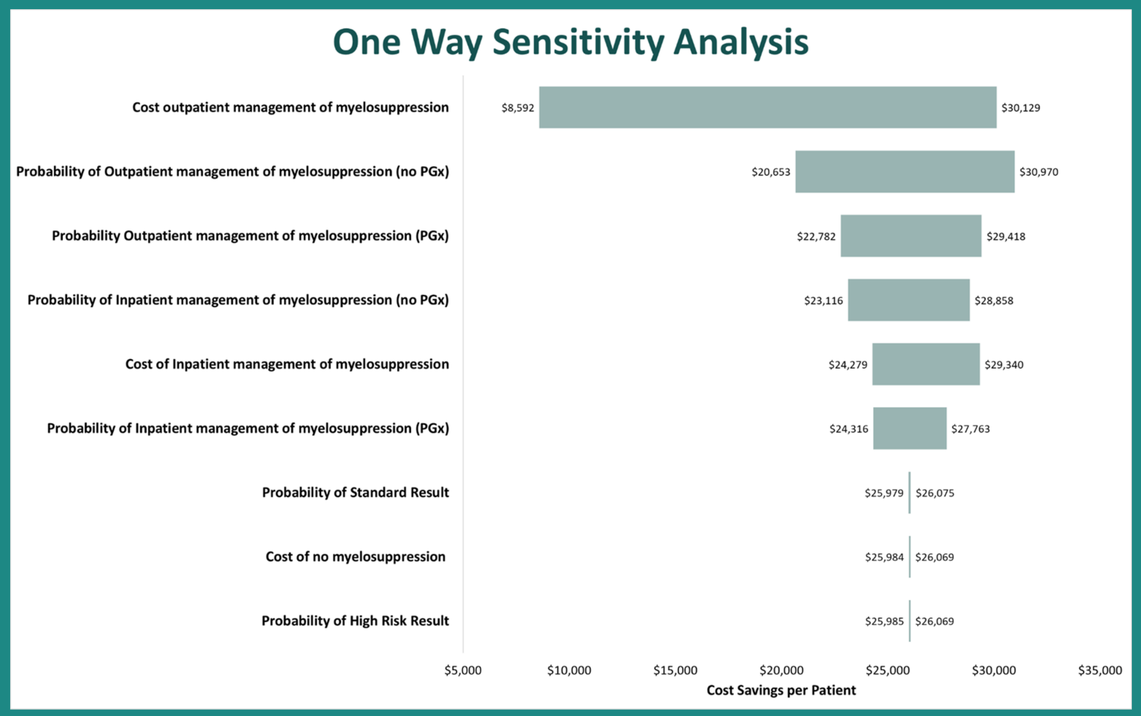

***Figure 2**. One-way sensitivity analysis for preemptive PGx testing vs. no PGx testing. Costs are shown in 2023 USD.*

The cost of outpatient management of moderate myelosuppression and likelihood of outpatient management of moderate myelosuppression in the no PGx testing group had the most significant impact on model results.

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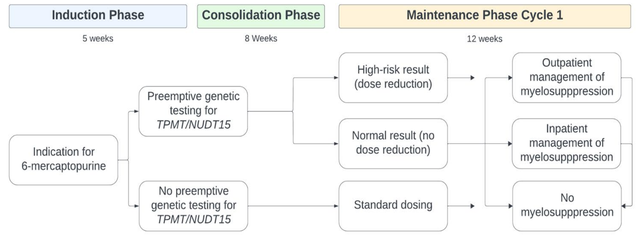

Figure 1. Markov model decision tree. High risk results refer to TPMT and/or NUDT15 intermediate, possible intermediate, and poor metabolizers. Normal result refers to TPMT and/or NUDT15 normal metabolizers. The model from "High-risk result" and "Standard dosing" proceeds the same way as "normal result".

In a hypothetical cohort of 1000 Black, Asian/Pacific Islander, White, and "Other" pediatric patients with ALL, a total of 157 patients were expected to have a TPMT or NUDT15 high-risk result (e.g. intermediate or poor metabolizer):
- 2 TPMT PMs
- 93 TPMT IMs
- 4 possible TPMT IMs
- 1 NUDT15 PM
- 55 NUDT15 IMs
- 4 possible NUDT 15 IMs[4,5]

CONCLUSION

- Preemptive PGx testing for *TPMT* and *NUDT15* results in **significant cost-savings** for pediatric ALL
- Educating healthcare providers and patients on PGx testing and the rationale behind dose adjustments is **crucial for the management of adverse drug reactions**
- Further studies should evaluate **logistics of implementing routine preemptive PGx testing** in clinical management

LIMITATIONS

- Assumed a time horizon of just 16 weeks
- Total cost of treatment for maintenance will be much more than estimated
- Assumed only one episode of myelosuppression would occur
- Severe myelosuppression accompanied by febrile neutropenia is extremely rare
- Medications involved in the course of therapy are dosed based on BSA
- Epidemiology of ALL reported across racial groups, CPIC genotype frequencies reported based on geographical sub-groups

REFERENCES

USC Mann Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences

Children's Hospital Los Angeles