Test Definition: BUAUC

Busulfan, Intravenous Dose, Area Under the Curve, Plasma

Overview

Useful For

Guiding dosage adjustments to achieve complete bone marrow ablation while minimizing dose-dependent toxicity

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
DOSE	Busulfan, IV Dose, AUC, P	No	Yes
BU2H	Busulfan, Immediate Post Infusion	No	Yes
BU3H	Busulfan, 1hr Post Infusion	No	Yes
BU4H	Busulfan, 2hr Post Infusion	No	Yes
BU6H	Busulfan, 4hr Post Infusion	No	Yes

Special Instructions

- Busulfan Information: Mail-In Specimen Instructions

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Heparin

Necessary Information

The time the drug administration is started and completed, the patient's dose (mg every 6 hours), body weight (kg), and age (years) must be submitted with the specimens. Without infusion start time, exact time of specimen collection, dose, and body weight, the area under the curve and clearance cannot be calculated. **Age is required for assessment of the correct dose per body weight**.

A completed Busulfan Information: Mail-In Specimen Instructions (T559) is required.

Specimen Required

Four plasma specimens with different collection times (keep all specimens under 1 order) are required.

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube: Green top (sodium heparin) (Plasma gel/PST are **not acceptable**)
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL Plasma
Collection Instructions:
1. The first specimen should be collected immediately after completion of the first intravenous infusion of 0.8 mg/kg busulfan.
2. Additional specimens should also be collected at 1 hour, 2 hours, and 4 hours after completion of infusion.
3. Label each specimen with exact time of collection.
4. Busulfan degrades quickly at ambient temperature. Specimens must be kept in wet ice slurry or refrigerated at 4 degrees C. Specimens must be centrifuged within 2 hours after collection. Separate the plasma and transfer to individual 5-mL plastic vials, labeled with exact time of collection. Immediately freeze at -20 degrees C.
Additional Information:
This test should only be ordered when the following criteria are met:
-Busulfan dosing protocol must be intravenous administration of 0.8 mg/kg doses every 6 hours over 4 days, for a total of 16 doses
Specimens must be collected as described below:
-1 specimen collected immediately after completion of the first 2-hour IV infusion of busulfan
-1 specimen collected 1 hour after the infusion is completed
-1 specimen collected 2 hours after the infusion is completed
-1 specimen collected 4 hours after the infusion is completed and prior to the next infusion of busulfan

Forms

1. **Busulfan Information: Mail-In Specimen Instructions (T559) is required**
2. If not ordering electronically, complete, print, and send a Therapeutics Test Request (T831) with the specimen.

Specimen Minimum Volume

Plasma: 0.25 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Heparin	Frozen (preferred)	28 days	
	Refrigerated	72 hours	

Clinical & Interpretive

Clinical Information

Busulfan is an alkylating agent used to ablate bone marrow cells prior to hematopoietic stem cell transplantation for chronic myelogenous leukemia.(1) Busulfan is typically administered intravenously (IV) at the recommended dosage of 0.8 mg/kg of actual or ideal body weight (whichever is lower) and given once every 6 hours over 4 days for a total of 16 doses. Dose-limiting toxicity of busulfan includes veno-occlusive liver disease, seizures, and coma. To avoid toxicity while ensuring busulfan dose adequacy to completely ablate the bone marrow, IV dosing should be guided by a pharmacokinetic (PK) evaluation of the area under the curve and clearance after the first dose.(2) The PK evaluation should be carried out at the end of the first dose, with results of PK testing available to facilitate dose adjustment before beginning the fifth dose.

Reference Values

AREA UNDER THE CURVE
900-1500 (mcmol/L)(min)

CLEARANCE
2.1-3.5 (mL/minute)/kg

Interpretation

Results of the timed collections will be used to calculate a 6-hour area under the curve (AUC). If a different dosing or specimen collection protocol is used, or if different calculations are required, contact the Laboratory Director.

The optimal result for AUC (6 hour) derived from this pharmacokinetic evaluation of IV busulfan is 1100 (mcmol/L)(min).

Area under the curve results greater than 1500 (mcmol/L)(min) are associated with hepatic veno-occlusive disease. A dose reduction should be considered before the next busulfan infusion.

Area under the curve results below 900 (mcmol/L)(min) are consistent with incomplete bone marrow ablation. A dose increase should be considered before the next busulfan infusion.

Clearance of busulfan in patients with normal kidney function is usually in the range of 2.1 to 3.5 (mL/min)/kg.

Elevated AUC is typically associated with clearance below 2.5 (mL/min)/kg, most frequently due to diminished activity of glutathione S-transferase A1-1 activity.(3)

Cautions

Failure to provide the 4 plasma specimens as described will invalidate the area under the curve calculations.

Clinical Reference

1. Santos GW, Tutschka PJ, Brookmeyer R, et al. Marrow transplantation for acute nonlymphocytic leukemia after treatment with busulfan and cyclophosphamide. N Engl J Med. 1983;309(22):1347-1353
2. Slattery JT, Sanders JE, Buckner CD, et al. Graft-rejection and toxicity following bone marrow transplantation in

relation to busulfan pharmacokinetics. Bone Marrow Transplant. 1995;16(1):31-42
3. Slattery JT, Risler LJ. Therapeutic monitoring of busulfan in hematopoietic stem cell transplantation. Ther Drug Monit. 1998;20(5):543-549
4. Czerwinski M, Gibbs M, Slattery JT. Busulfan conjugation by glutathione S-transferases alpha, mu, and pi. Drug Metab Dispos. 1996;24(9):1015-1019
5. Vassal G, Re M, Gouyette A. Gas chromatographic-mass spectrometric assay for busulfan in biological fluids using a deuterated internal standard. J Chromatogr. 1988;428(2):357-361
6. Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 12th ed. Biomedical Publications; 2020
7. Busulfex. Package insert. Otsuka Pharmaceutical Co, Ltd; Updated January 2015. Accessed October 8, 2024. Available at www.accessdata.fda.gov/drugsatfda_docs/label/2015/020954s014lbl.pdf
8. Palmer J, McCune JS, Perales MA, et al. Personalizing busulfan-based conditioning: considerations from the American Society for Blood and Marrow Transplantation Practice Guidelines Committee. Biol Blood Marrow Transplant. 2016;22(11):1915-1925

Performance

Method Description

Busulfan analysis is performed by liquid chromatography tandem mass spectrometry with calculation of area under the curve (AUC) by integration of the time versus concentration curve from start of infusion to last specimen collection (6-hour AUC).(Unpublished Mayo method)

The AUC and clearance are calculated after quantification of busulfan concentration in plasma samples collected at specific time points after the initial infusion. The AUC is calculated by integration of the plot of time in minutes from the start of infusion until the last specimen collection (independent variable), with busulfan concentration in mcmol/L (dependent variable) and straight-line extrapolation of the immediate postinfusion busulfan concentration to time zero. Clearance is calculated as the dose divided by AUC.

The recommended optimal dose is calculated based on the assumption of an ideal AUC=1100 mcmol*min.(Slattery JT, Risler LJ. Therapeutic monitoring of busulfan in hematopoietic stem cell transplantation. Ther Drug Monit. 1998;20[5]:543-549)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

Same day/1 to 3 days

Specimen Retention Time

14 days

Test Definition: BUAUC

Busulfan, Intravenous Dose, Area Under the Curve, Plasma

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

80299 x 4

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BUAUC	Busulfan, IV Dose, AUC, P	93478-6

Result ID	Test Result Name	Result LOINC® Value
DRDT2	Draw Date	33882-2
DRTM2	Draw Time	49049-0
24221	Busulfan result	93436-4
DRDT3	Draw Date	33882-2
DRTM3	Draw Time	49049-0
24222	Busulfan result	93435-6
DRDT4	Draw Date	33882-2
DRTM4	Draw Time	49049-0
24223	Busulfan result	93434-9
DRDT6	Draw Date	33882-2
DRTM6	Draw Time	49049-0
24224	Busulfan result	93433-1
DSE	Initial Dose	93477-8
DAT16	Infusion Start Date	88063-3
TM82	Infusion Start Time	88060-9
DAT17	Infusion Stop Date	88062-5
TM65	Infusion Stop Time	88061-7
W8	Weight	29463-7
24220	Age	30525-0

24225	Area Under the Curve, (0-6 Hour)	93476-0
24226	Clearance	93475-2
24227	Recommended Dose	93477-8