MAYO CLINIC LABORATORIES

Test Definition: USTEK

Ustekinumab Quantitation with Antibodies, Serum

Overview

Useful For

Evaluation of loss of response to therapy

Quantification of ustekinumab in human serum

Trough level quantitation for evaluation of patients treated with ustekinumab

Detection of antibodies to ustekinumab in human serum

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
USQN	Ustekinumab QN, S	No	Yes
USTAB	Ustekinumab Ab, S	No	Yes

Testing Algorithm

For more information see Ulcerative Colitis and Crohn Disease Therapeutic Drug Monitoring Algorithm.

Special Instructions

- Ulcerative Colitis and Crohn Disease Therapeutic Drug Monitoring Algorithm

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top

Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Collection Instructions:
1. Draw blood immediately before the next dose of drug administration (trough level).
2. Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send 1 of the following with the specimen:
-Gastroenterology and Hepatology Test Request (T728)
-Therapeutics Test Request (T831)

Specimen Minimum Volume

0.35 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK
Heat-inactivated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	21 days	
	Frozen	21 days	

Clinical & Interpretive

Clinical Information

Ustekinumab (UTK) is a fully human IgG1 kappa monoclonal antibody (1) that binds with high affinity to the p40 subunit of human interleukin (IL)12 and IL23 and has been approved for the treatment of patients with moderate to severe Crohn disease (CD), moderate to severe ulcerative colitis (UC), psoriatic arthritis, and plaque psoriasis. The drug prevents IL12 and IL23 bioactivity by binding and neutralizing the shared p40 subunit, preventing interaction with the cell surface receptor protein IL12Rbeta1. Through this mechanism of action, UTK effectively neutralizes IL12 and IL23, proteins that are thought to be associated with gastrointestinal inflammation in CD and UC. In the setting of the inflammatory bowel diseases (IBD), CD and UC, the treatment regimen is started with a single weight-based loading dose of the t-mab administered intravenously (IV), and a maintenance regimen with standard (non-weight based) subcutaneous administration of ustekinumab 8 weeks after induction dose, and every 8 weeks thereafter. There is very little data supporting proactive therapeutic drug monitoring for ustekinumab.

This test is most useful in the evaluation of loss of response to therapy. A gradual decrease in efficacy over time following an initial response to biologics is common. In many cases, antibodies generated to the biologic are responsible for treatment failure, as they bind to the drug creating an immunocomplex and clear the drug faster from circulation.

For IBD, measurements in nonresponders are indicated at post-induction (week 8) and concentrations of ustekinumab associated with favorable outcomes are greater than 3.5 mcg/mL. In addition, for measurements during maintenance stages of therapy, ustekinumab concentrations greater than or equal to 1 mcg/mL are associated with clinical response and clinical remission. At maintenance stages, ustekinumab concentrations greater than or equal to 4.5 mcg/mL are associated with mucosal healing.

In clinical trials, 6% to 12.4% of patients using ustekinumab for psoriasis or psoriatic arthritis developed antibodies-to-ustekinumab (ATU) over time. For IBD, between 2.9% and 4.6% of patients developed ATU when treated with ustekinumab for 1 year.(1) Therefore, it is important to monitor trough concentrations of serum UTK to correlate drug levels with loss of response to therapy. ATU may increase drug clearance in treated patients or neutralize the drug effect, thereby potentially contributing to the loss of response. ATU could also cause adverse events, such as serum sickness and hypersensitivity reactions.

Currently, ustekinumab quantitation is performed in conjunction with immunogenicity assessment for ATU.

Reference Values

USTEKINUMAB QN, S:
Limit of quantitation is 0.3 mcg/mL

In inflammatory bowel disease, at post-induction measurement (week 8), concentrations above 3.5 mcg/mL are associated with good outcomes.

For maintenance stages:
Concentrations > or =1.0 mcg/mL are associated with clinical response and clinical remission
Concentrations > or =4.5 mcg/mL are associated with mucosal healing

USTEKINUMAB AB, S:
Limit of quantitation is 10 AU/mL
Absent: <10 AU/mL
Present: > or =10 AU/mL

Interpretation

	Antibodies to ustekinumab (ATU) absent	ATU present
Ustekinumab quantification <1.0 mcg/mL	For nonresponders: Insufficient ustekinumab is present. In the absence of ATU, consider optimizing therapy by increasing the dose or shortening the administration	For nonresponders: Insufficient ustekinumab is present. Antibodies-to-ustekinumab detected can contribute to faster clearance of ustekinumab and treatment failure.

	intervals, or by adding an immunomodulator to the therapeutic regimen.	Clinical evaluation is recommended.
Ustekinumab quantification > or =1.0 mcg/mL	For nonresponders: If the sample was collected at trough ie, immediately before the next infusion, the results could suggest a mechanistic failure of ustekinumab. The provider may consider switching therapeutic regimen outside of the drug class.	For nonresponders: If the sample was collected at trough ie, immediately before the next infusion, the results could suggest a mechanistic failure of ustekinumab. The provider may consider switching therapeutic regimen outside of the drug class.

Cautions

This assay measures free ustekinumab (UTK) and free antibodies to ustekinumab (ATU). This assay does not measure UTK bound to ATU (immunocomplexes).

Presence of UTK at concentrations greater than 1 mcg/mL may impair detection of ATU, as the ATU assay is not drug tolerant.

Elevated rheumatoid factor (RF) may falsely increase results of ATU. During validation studies, negative ATU samples remained negative and positive ATU samples remained positive; however, the quantitative result differed by more than 20% when compared to the non-RF spiked original samples. If patients are positive for RF, clinical correlation is recommended for ATU test interpretation.

Clinical Reference

1. Stelara (ustekinumab). Package insert: Prescribing information. Janssen Pharmaceuticals; revised 03/2020
2. Papamichael K, Cheifetz AS, Melmed GY, et al. Appropriate therapeutic drug monitoring of biologic agents for patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol. 2019;17(9):1655-1668.e3

Performance

Method Description

Ustekinumab (UTK) quantitation and anti-ustekinumab antibody measurements are performed using enzyme-linked immunosorbent assay. Microwell strips are pre-coated with UTK or anti-UTK antibody . Calibrators, controls, and patient samples are added to separate wells, allowing either UTK or antibodies to ustekinumab (ATUs) to bind to immobilized antigen. Unbound sample is washed away, and a second horseradish peroxidase-labeled anti-UTK or UTK (conjugate) is added to each well. A second incubation step allows the conjugate to bind to the UTK or ATU that has become attached to the microwells. After washing away the excess of unbound conjugate, the remaining enzyme activity is determined by adding a substrate and measuring the intensity of the color that develops in a spectrophotometer. The signal obtained is proportional to the amount of UTK or ATUs in the patient sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed
Monday, Wednesday, Friday

Report Available
2 to 5 days

Specimen Retention Time
14 days

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
83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
USTEK	Ustekinumab QN with Antibodies, S	In Process

Result ID	Test Result Name	Result LOINC® Value
USQN	Ustekinumab QN, S	87408-1
USTAB	Ustekinumab Ab, S	87409-9