The PartoSure test is a rapid, qualitative test for detecting the presence of placental alphal microglobulin-1 (PAMG-1) in cervicovaginal secretions. The device is indicated as an aid to rapidly assess the risk of spontaneous preterm delivery ≤ 7 days from the time of cervicovaginal sample collection in pregnant women with signs and symptoms of early preterm labor, intact amniotic membranes and minimal cervical dilation (≤ 3 cm), sampled between 24 weeks, 0 days and 34 weeks, 6 days gestation in women with a singleton gestation.

**SUMMARY AND EXPLANATION OF THE TEST**

An accurate risk assessment of spontaneous preterm delivery ≤ 7 days is clinically important among pregnancies with signs or symptoms suggestive of preterm labor. This is particularly true with respect to both the administration of corticosteroids, which have an optional benefit ≤ 7 days of administration,1 as well as the transfer of a patient to a tertiary care center capable of caring for the birth of a premature infant. Placental alphal microglobulin-1 (PAMG-1), a protein released from decidual cells into the amniotic cavity throughout pregnancy, was first described by Petrunin et al. in 1975.2 PAMG-1 is not found in the extracellular matrix surrounding the amniotic cavity, which theoretically reduces the opportunity for its unnecessary release into the vaginal cavity due to cervical distortions caused by digital examinations. The PartoSure test provides a simple sample collection option for clinicians to assess the risk of spontaneous preterm delivery ≤ 7 days in women with a singleton gestation with the benefit of being a rapid, point-of-care test, performed with a simple sample collection procedure that does not require a spectrom analysis or specialized equipment for sample analysis. Its presence in cervicovaginal discharge when labor and delivery are imminent is likely due to the transudation of the protein through pre-existing pores in the chorionicamniotic membranes during uterine contractions and, potentially, degradation of the extracellular matrix of fetal membranes to an inflammatory process of labor.3 The clinical utility of a rapid and reliable test result based on a specimen collected non-invasively at the point of care represents an additional option to identify preterm labor that may result in spontaneous preterm delivery ≤ 7 days of testing among women with a singleton gestation.

**PRINCIPLE OF THE TEST**

PartoSure is a lateral flow, immunochemotach assay designed to identify the presence of human placental alphal microglobulin-1 (PAMG-1). The test employs monoclonal antibodies sufficiently sensitive to detect 1 ng/mL of PAMG-1. For the analysis, a sample of cervicovaginal discharge collected by vaginal swab is extracted into a solvent. The presence of PAMG-1 antigen is then determined by inserting a lateral flow test strip into the vaginal swab. The sample flows from an absorbent pad to a nitrocellulose membrane, passing through a reactive area containing monoclonal anti-PAMG-1 antibodies conjugated to a gold particle. The antigen-antibody complexes flow to the test region where it is immobilized by a second anti-PAMG-1 antibody. This event leads to the appearance of the test line. Unbound antigen-antibody complexes flow to flow along the test strip and are immobilized by a second antibody. This leads to the appearance of the internal control line.

**REAGENTS AND COMPONENTS**

The PartoSure test kit includes the following components: The PartoSure test strip in a foil packet with desiccant, a sterile flocked vaginal swab, and a plastic vial with solvent solution (0.9% NaCl, 0.05% NaN₃, 0.01% Triton X100). Sodium azide may react with substances if suspected to be present.

**STORAGE AND STABILITY**

Store the PartoSure test kit in a dry place at 15 to 25°C (59 to 77°F). The test strip should not be frozen.

**TEST PROCEDURE**

1. Take the solvent vial by its cap and ensure all liquid in the vial has dropped to the bottom. Open the solvent vial and place it in a vertical position.

2. To collect a sample from the vagina, use only the sterile flocked swab provided with the PartoSure test kit. Remove the swab from its package following the instructions on the packaging. The tip of the swab should not be allowed to touch insertion into the vagina. Hold the swab by its neck, and while the patient is lying on her back, carefully insert the tip of the swab into the vagina until the fingers contact the skin (no more than 2-3 inches or 5-7 cm deep). Withdraw the swab from the vagina after 30 seconds.

3. After the swab has been removed from the vagina, immediately place the tip into the provided solvent vial and rinse by rotating for 30 seconds.

4. Remove the swab from the vial and dispose of it.

5. Tear open the foil pouch at the tear notches and remove the PartoSure test strip.

6. Insert the white end of the test strip (marked with arrows facing downward) into the vial with solvent.

7. Remove the test strip from the vial if two lines are clearly visible in the test region or after 5 minutes sharp. Read the results by placing the test strip on a clean, dry flat surface in a well-lit environment via either natural or fluorescent lighting. A positive result is indicated by two lines in the test region, while a negative result is indicated by a single line in the test region. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

8. The intensity of the lines may vary; the test result is valid even if the lines are faint or uneven. Do not interpret the test result based on the intensity of the lines. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

**PRECAUTIONS AND WARNINGS**

- Use of any swab or solvent solution other than the one provided with the test kit is prohibited.

- Samples should be collected prior to collection of culture specimens.

- The PartoSure test is for in vitro diagnostic use only and no component of the test should be taken internally.

- Do not use the kit if the swab or test strip package integrity is compromised or if the solvent vial has leaked.

- Do not bend or fold the test strip or the foil pouch with the test strip in it; doing so may damage the strip and lead to inaccurate results.

- The PartoSure test includes a plastic vial with solvent solution (0.9% NaCl 0.05% NaN₃ 0.01% Triton X100). Sodium azide may react with plumbing to form potentially explosive metal azides. Avoid contact with skin, eyes, and clothing. In case of contact with any of these reagents, wash area thoroughly with water. If disposing of this reagent, always flush the drain with large volumes of water to prevent azide build up.

- Safety precautions should be observed when collecting, handling, and disposing of test samples.

- Used test kits are biohazardous; dispose of all components using necessary precautions.

**QUALITY CONTROL**

The PartoSure test strip contains an internal procedural control mechanism that ensures analytical functionality. The appearance of one or two lines in the results region of the test strip verifies the integrity of the test procedure and components.

**EXPECTED VALUES**

The PartoSure test detects traces amounts of human PAMG-1. Patient specimens with a concentration of 1 ng/mL placental alpha microglobulin-1 (PAMG-1) or greater will result in a positive PartoSure test. This clinical cutoff was determined using a risk-based approach based on the maximum background concentration of PAMG-1 (0.22 ng/mL) in cervicovaginal secretions to optimize the performance of the PartoSure test. This approach was subsequently validated in a pivotal study including 686 subjects of the intended use population across 15 clinical sites in the United States, and a real-world data study including 511 subjects of the intended use population in one European site.
SAMPLE COLLECTION AND TEST PROCEDURE

To collect a sample from the vaginas, use only the sterile flocked swab provided with the PartoSure test kit. Remove the swab from its package following the instructions on the packaging. The tip of the swab should not touch anything prior to insertion into the vagina. Hold the swab by the middle of its shaft and, while the patient is lying on her back, carefully insert the tip of the swab into the vagina until the fingers contact the skin (no more than 2-3 inches). A penetration depth measurement is not required. Withdraw the swab from the vagina after 30 seconds. After the swab has been removed from the vagina, immediately place the tip into the provided solvent vial and rinse by rotating for 30 seconds. Remove the swab from the vial and dispose of it. Tear open the foil pouch at the tear notches and remove the PartoSure test strip. Insert the tip of the test strip (marked with arrows facing downward) into the vagina with solvent. Remove the test strip from the vagina if two lines are clearly visible in the test region or after 5 minutes short. Read the results by placing the test strip on a clean, flat surface. A positive result is indicated by two lines in the test region, while a negative result is indicated by a single line in the test region. If the control line does not appear (i.e., no lines appear or only the test line appears), then the result is invalid. In the event of an invalid test result, collect a new sample and then retest. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vagina. The intensity of the lines may vary; the test result is valid even if the lines are faint or uneven. Do not interpret the test result based on the intensity of the lines. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vaginal test results may occur if the collection swab is contaminated by lubricants or antiseptics (e.g. K-Y® or Surgilube® lubricating jelly, Betadine® Cleaner).

CROSS REACTIVITY

The PartoSure test was evaluated using a panel of potentially cross-reactive human neogen substrates. Each of the seven specimens included human chorionic gonadotropin, trophoblastic beta-2 glycoprotein, human placental lactogen, alpha-fetoprotein, GBS-F3P, and human serum albumin. Each of the seven specimens was tested against a high negative sample (0.2 ng/mL), a high positive (0.5 ng/mL), the limit of detection (1.0 ng/mL), a low positive (2.0 ng/mL), and two concentrations within the 0.2 and 2.0 ng/mL regions for the detection of 0.5 ng/mL and 0.9 ng/mL. The results of this study demonstrated 100% negative results at ≤0.5 ng/mL and 100% positive readings at ≥1 ng/mL for the PAMG-1 levels by intended users.

Safety & Effectiveness

The results of two large clinical studies have been used to demonstrate the safety and the times of the PartoSure test as an aid in assessing the risk of spontaneous preterm delivery ≤7 days of testing among women with a singleton gestation and signs and symptoms of preterm labor. A spontaneous preterm delivery was defined as delivery occurring subsequent to spontaneous onset of preterm labor, preterm premature rupture of membranes, or fetal membrane prolapse, regardless of subsequent labor augmentation or cesarean delivery. In the first study (US Study), which was a large, multi-center, prospective cohort study, 686 women with a singleton gestation were evaluated at 15 clinical sites across the United States. From these study data, it was determined that the expression of placental alpha microglobulin-1 (PAMG-1) in the vaginal secretions can be used to assess the risk of spontaneous preterm delivery ≤7 days of specimen collection among symptomatic pregnant women with a singleton gestation and signs and symptoms of preterm labor. In the second study (European Study), which was a prospectively conducted, retrospective cohort study evaluating the performance of the PartoSure test using prospectively collected vaginal swabs from hospital in Europe, 511 women with a singleton gestation were evaluated from these data. It was determined that the findings of the two prospective cohort studies are supported by the real-world performance of the PartoSure test.

In both studies, the PartoSure test specimen was collected prior to cervical digital examination from symptomatic pregnant women with a singleton gestation meeting the following clinical criteria:

- Have signs and symptoms of threatened preterm delivery limited to:
  - Urine contractions (with or without pain)
  - Intermittent lower abdominal pain, dull backache, pelvic pressure
  - Vaginal bleeding during the second or third trimester (rhematome)
  - Menstrual-like intestinal cramping (with or without diarrhea)
  - Change in vaginal discharge (amount, color, or consistency)

- Have a gestational age between 24 weeks, 0 days and 34 weeks, 6 days
- Have intact amniotic membranes
- Have minimal cervical dilation (< 3 centimeters)

The positive and negative predictive values (PPV/NPV) of the PartoSure test provide additional information subsequent to preterm delivery ≤7 days in both studies are shown in Table 2.

Table 2. PartoSure PPV & NPV for the Prediction of Spontaneous Preterm Delivery ≤7 Days Among Symptomatic Women with a Singleton Gestation (n=1,117)

<table>
<thead>
<tr>
<th>US Study</th>
<th>PTD ≤ 7 Days</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Proportion</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Positive Predictive Value (PPV)</td>
<td>3/14</td>
<td>(47.5, 50.8)</td>
</tr>
<tr>
<td>Negative Predictive Value (NPV)</td>
<td>669/672</td>
<td>99.6</td>
</tr>
<tr>
<td>European Study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>Proportion</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Positive Predictive Value (PPV)</td>
<td>9/29</td>
<td>(31.3, 50.5)</td>
</tr>
<tr>
<td>Negative Predictive Value (NPV)</td>
<td>473/482</td>
<td>98.1</td>
</tr>
</tbody>
</table>

For spontaneous preterm delivery ≤7 days in symptomatic women with a singleton gestation, the PPV & NPV of the PartoSure test from the US and the European Studies were 21.4% and 99.6%, and 31.0% and 98.1%, respectively. The prevalences of spontaneous preterm delivery ≤7 days among women with a singleton gestation in the US and European Studies were 0.9% and 3.5%, respectively.

Additional Performance Characteristics

The sensitivity and specificity of the PartoSure test from the US and European Studies for spontaneous preterm delivery ≤7 days were 99.2% (95% CI 98.8, 99.5) and 21.4% (95% CI 16.0, 27.4) and 99.5% (95% CI 93.8, 97.5), respectively. Symptomatic patients with a negative PartoSure test are still at increased risk for spontaneous delivery within 7 days of test date whether they present for unscheduled care. It is critical to recognize that PAMG-1 is only one marker of preterm delivery and is not present in elevated levels in patients with other causes of delivery. All women with a positive PartoSure test should be delivered ≤7 days of testing. Table 3 provides the 2x2 performance tables in both the US and European studies.

Table 3. PartoSure Test 2x2 Performance Tables (n=1,117)

<table>
<thead>
<tr>
<th>US Study</th>
<th>PPV &amp; TPT ≤ 7 Days</th>
<th>Total</th>
</tr>
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<tbody>
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<td>Negative Predictive Value (NPV)</td>
<td>669/672</td>
<td>99.6</td>
</tr>
</tbody>
</table>

In the US study, of the 6 spontaneous preterm deliveries ≤7 days, 3 were predicted by the PartoSure test (i.e., true positives) and 3 were missed by the PartoSure test (i.e., false negatives). In the European study, of the 18 spontaneous preterm deliveries ≤7 days, 9 were predicted by the PartoSure test (i.e., true positives) and 9 were missed by the PartoSure test (i.e., false negatives).

CLINICAL SIGNIFICANCE OF THE PARTOSURE TEST

Evidence supporting the efficacy of the PartoSure test has been limited to observational studies establishing the association between the test result and likelihood of spontaneous preterm delivery ≤7 days. Because no randomized controlled studies have yet been completed to determine the therapeutic efficacy of using the PartoSure test in conjunction with other clinical information for the treatment or prevention of threatened preterm delivery, it is not possible to make recommendations regarding specific treatment options.

Management of Women with a Positive PartoSure Test Result

Management decisions should always be made in conjunction with other available clinical information to avoid unnecessary interventions such as bedrest, in-utero transfers, hospitalizations, and medication administration.

Management of Women with a Negative PartoSure Test Result

While pregnant women with symptoms of preterm labor and a singleton gestation have a pre-test probability as low as 0.9% of spontaneous delivery ≤7 days of specimen collection, those with a negative PartoSure test result have as low as a 0.4% probability of delivering spontane ous ≤7 days. Despite this low probability, it is important to always consider a negative PartoSure test result in conjunction with all other information provided by the patient’s clinical evaluation and diagnostic procedures, as well as the circumstances surrounding her condition, including her activity, and evaluation of other risk factors. Patient education regarding her risk of preterm delivery given her symptoms as well as continued vigilance surrounding her condition should remain critical components of her management plan.

ROLE OF PARTOSURE IN IDENTIFYING DELIVERY RISK

The PartoSure test should always be used in conjunction with other clinical risk factors and information to assess overall risk of imminent spontaneous preterm delivery, thus allowing for appropriate patient management. The PartoSure test is an aid in assessing the risk of spontaneous preterm delivery ≤7 days from the time of cervical/augmentation in pregnant women with a singleton gestation and signs and symptoms of early labor.

BIBLIOGRAPHY