6P-An Innovative Evidence-Based Laboratory Medicine (EBLM) Test to Help Doctors in the Screening of Ovarian Cancer

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Background

- **Ovarian cancer (OC)** is the seventh most common cancer among women and ranks eighth in terms of cancer-related deaths in women. Despite its relatively low incidence, its impact is significant because it is **often diagnosed at a late stage and has limited treatment options (Figure 1)**.

Incidence[1]:
6.7%, 300,000 people

Mortality[1]:
4.0%, > 200,000 people

Figure 1. Global incidence and mortality of ovarian cancer

- The **main risk factors of OC** are age, obesity, birth control, fertility drugs, estrogen or hormone replacement therapy, endometriosis, polycystic ovarian syndrome, family history of ovarian cancer, breast cancer, or colorectal cancer, among others **(Figure 2).**

Endometriosis[2]:
10% Women, 190 M people

Polycystic ovarian syndrome (PCOS)[2]:
8-13% women of childbearing age, 4 M people

Breast cancer (BC)[1]:
46,8%, > 2 M people

Colorectal cancer (CRC)[1]:
18.4%, almost 2 M people

Figure 2. Global incidence of major risk factors for ovarian cancer

- Named the **'silent killer'** for its vague symptoms, ovarian cancer often leads to delayed diagnosis and metastasis. Hence, early detection remains challenging.
- **Survival** in ovarian cancer is strongly **associated with tumor stage at diagnosis**:

5-YEAR SURVIVAL RATES

Detected at:

EARLY STAGES
Stage I – 89%
Stage II – 71%

LATE STAGES
Stage III – 41%
Stage IV – 20%

- Suspected OC involves a physical exam, followed by an ultrasound if an enlarged ovary or ascites is detected. Upon detection of an adnexal mass, malignancy is confirmed on biopsy samples.
- Most cases of suspected OC are not cancerous and unrelated to OC. Each year in the U.S., nearly 300,000 ovarian masses are removed, most of them unnecessarily.
- Hence, alternative, **accurate and non-invasive strategies** for OC **early detection** are needed.
- This study aims to develop a diagnostic tool that accurately **detects OC, even in early stages**, before symptoms appear and when treatment is most likely to succeed.

Objective:

To develop and evaluate the accuracy of a novel **non-invasive test** for ovarian cancer early detection.

Methods

- This **disruptive blood and urine-based screening test** is designed specifically based on **serum biomarkers for ovarian cancer screening:**

Analyzed parameters

Serum Hepatic Enzymes
ALP, AST, ALT, GGT, LDH

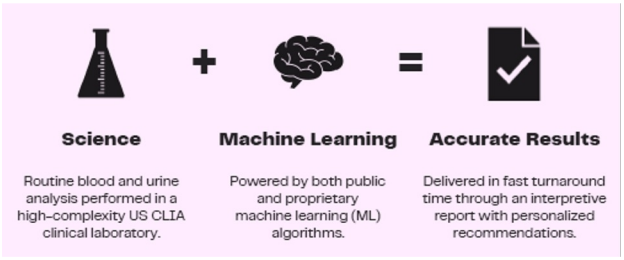
Other Serum Analytes
Creatinine
Bilirubin (total and direct)

Other Clinical Data
Age, gender, ethnicity, anthropometric data, blood pressure and lifestyle habits

Serum Tumor Markers
CA 19.9, CA 125, CEA, HE4

Urine Analytes
Albumin
Creatinine

- To assess the estimated accuracy of our test, we conducted an **extensive literature review** of constituent algorithms, calculations and analyte combinations included in diagnostic accuracy studies.
- Parallel and serial approximations were conducted to optimize overall **sensitivity (Se)** and **specificity (Sp)**, respectively, a process performed by our own **machine learning (ML) algorithm (Figure 3)**.



US: United States; CLIA: Clinical Laboratory Improvement Amendments

Figure 3. How the test works

Results

Sample Size:
9,324 subjects

ACCURACY OF THE TEST (IC 95%):

- **Sensitivity, 0.97** and **Specificity, 0.93.**
- Approximation of the **Area under the receiver operating characteristic (AUROC)** curve, **0.92.**
- Estimation of the **Positive predictive value (PPV), 0.93.**
- Estimation of the **Negative predictive value (NPV), 0.97.**

Conclusions

- This data suggests that the innovative non-invasive blood-based biomarker algorithm **holds promise in providing timely ovarian cancer screening**, particularly among individuals aged 40 and above.
- We are conducting an extensive parallel study with additional analytes to increase the sample size, the sensitivity and the specificity of the test and offer the physicians a tool with minimum false negatives (FN) results.

Disclosures: J. D. Santotoribio has no conflicts of interest to declare. S. J. Calleja is a shareholder of Kience and Blueberry Diagnostics.

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