Department of Health and Human Services

FDA Perspective: Analytical Aspects of CA-125 Tests

Ovarian Cancer End Points Workshop

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FDA

In the Beginning…

- Centocor RIA – 1987
- Class III, Premarket Application, Panel Track
- Safety and Effectiveness
- "…use as an aid in the detection of residual ovarian carcinoma in patients who have undergone first-line therapy and would be considered for second look…"

Down Classification in 1997

- Class II, 510(k) submissions
- Guidance Document for Tumor Associated Antigens (1996)
- Substantially equivalent
- 8 manufacturers, 16 devices
- "…aid in management…aid in monitoring response…serial testing…detection of cancer recurrence…use in conjunction with other clinical methods…"

Technologies

- Calibrators provided (if not a gold standard, at least continuity and a small community)
- Immunologic assay – dual antibody (monoclonal, polyclonal or both)
- Solid phase – usually beads (pulled, spun, strained)
- Light-based read-out – chemiluminescence, fluorimetry

Analytical Performance Characteristics

- Units roughly comparable. Regression slope examples: 1.34, 1.20, 1.06, 1.03, 1.01, .99, .97, .96, .96, .77
- Uniformly high correlations: .95 to .99
- Well-reproducible results. Tests' total CV's range from 2.7% to 6.9%
- Dynamic range an issue?

Positive/Negative Assay Concordances

Positive	Negative	Overall
.77	.61	.68
.96	.99	.98
.98	.97	.97
.98	.97	.97

Correlations with Clinical Progression

Sensitivity	Specificity	Efficiency
.84	.84	.84
.82	.89	.87
.95	.22	.71
.95	1.00	.98
.52	.88	.76
.92	.64	.73

Why the Variability?

- Same ROC, different cut-offs? Not by design, but maybe imposed by varying responsivity?
- Different specifications for test change or trend?
- No gold standard for change in the disease.
- Small patient sets
  - Differing populations
  - Random noise
  - Post hoc fitting

Thinking of CA-125 as an SEB?

- Know your test.
  - Read the label.
  - Read beyond the label.
- Pick a test and stay with it.
- Fully define the criteria for interpreting change or trend in test results.
- Characterize, as well as possible, test interactions with other clinical features.