Osteopontin as a Diagnostic biomarker in cancer research - Analysis using GOBIOM database

GVK BIO
Accelerating Research

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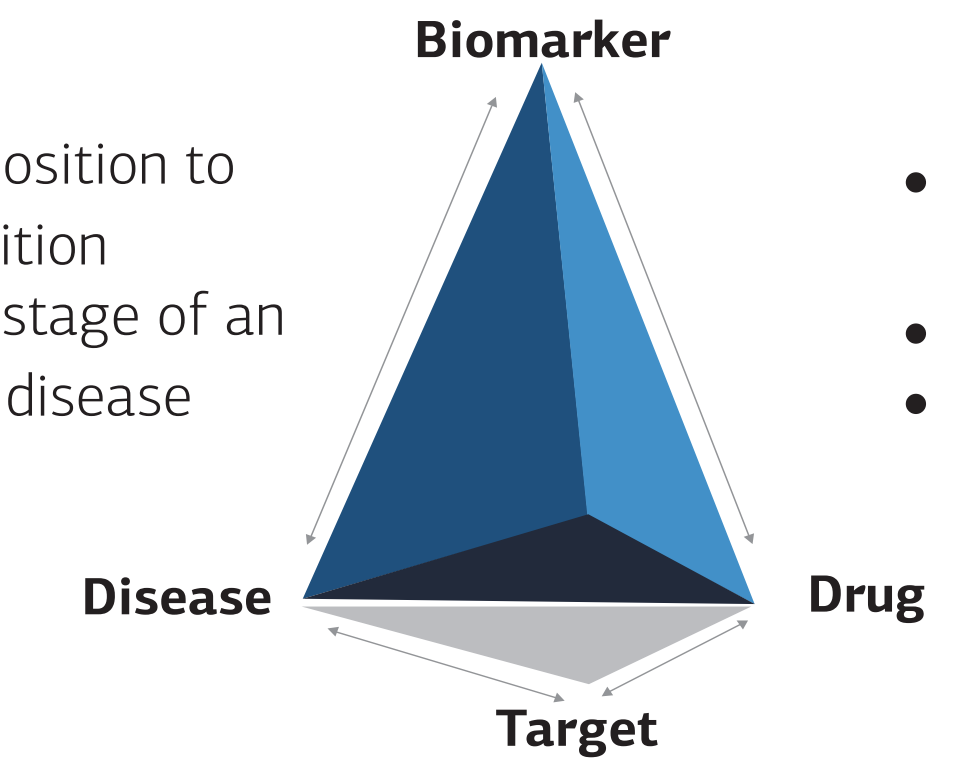
Introduction

- Overexpression of Osteopontin (OPN), the extracellular matrix protein, is emerging as a promising marker for multiple cancers
- Multiple and complex mechanisms are involved in the role of osteopontin in cancer, including interactions with cell surface receptors, growth factor/receptor pathways, and proteases
- Several contradictory studies are reported over the extent of OPN overexpression and its relation to the malignancy
- Aim of the study was to analyze the literature that is published on OPN as a biomarker for multiple cancers and establish its association with a single disease to which it is highly sensitive compared to others
- To do the analysis, we used the data from GVK BIO Online Biomarker Database (GOBIOM), which is a repository of all clinical, preclinical and exploratory biomarkers reported for various indications

GOBIOM
GVK BIO Online Biomarker Database

- GOBIOM database is developed by GVK BIO in collaboration with USFDA and a Big Pharma
- Currently, GOBIOM has information on 13,277 known biomarkers for 551 indications with 55,625 references. Data is manually curated from
  - Clinical Trial Registries
  - Validated clinical trial results from pharma companies
  - Scientific Conferences
  - Published Literature and other web resources
- Database gives information on the details of the clinical study in which a biomarker is measured along with its reported utilities like diagnosis, prognosis, monitoring disease progression, treatment response, surrogate, efficacy and toxicity
- A proprietary Tetrahedron model is adopted in the framework of the database by linking biomarkers, therapeutic area, Drug and the Target. This model simplifies the process of biomarker data analysis using GOBIOM

The Conceptual Framework



- A preposition to disposition
- Some stage of an active disease

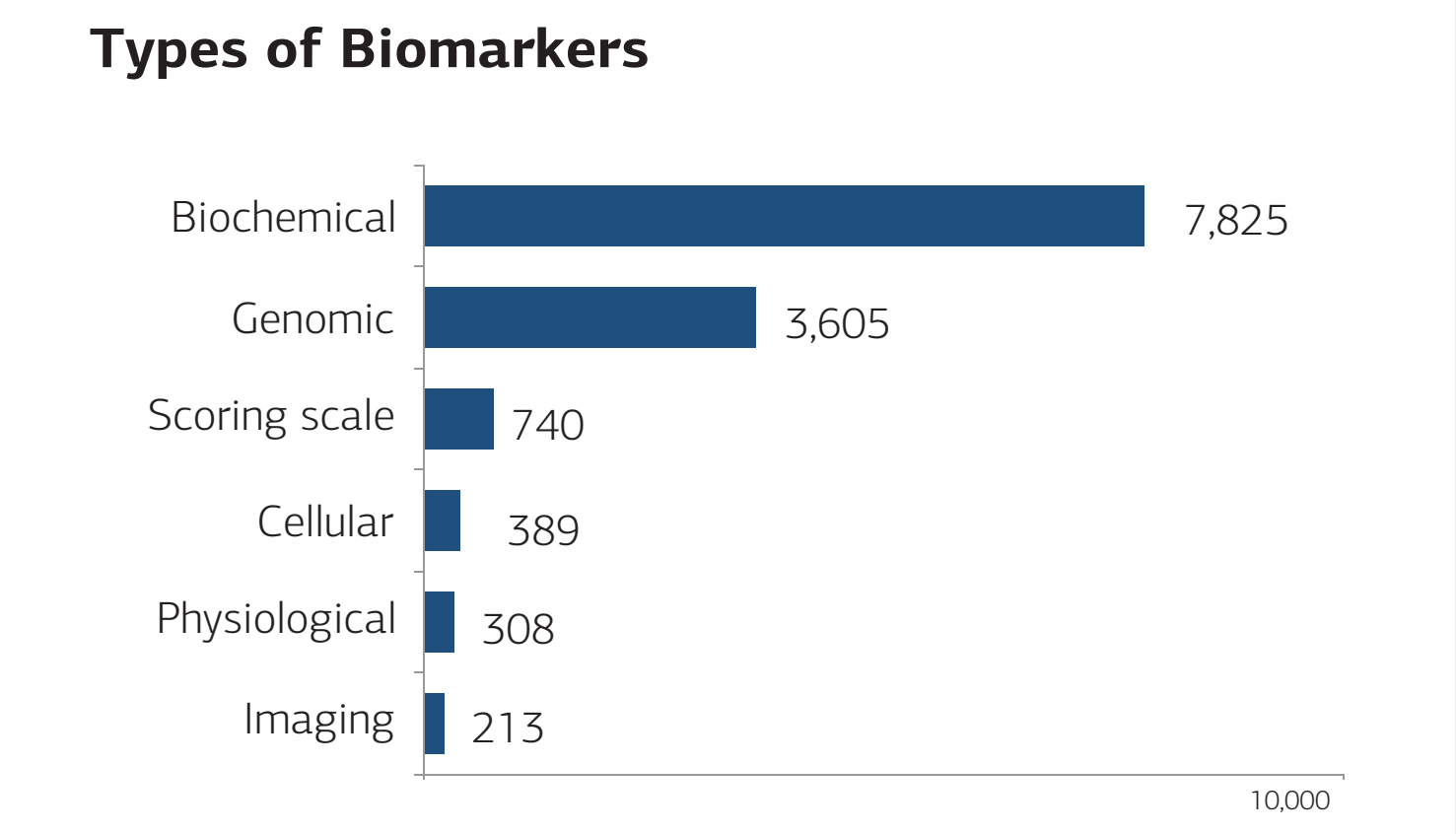
- On target / off-target effects
- PK / PD Profiles
- Down-stream signaling cascade

The Proprietary Tetrahedron database model evolved in conjunction with relevant industry participants, allows the user in understanding the complexity of the process involved in biomarkers discovery and validation.

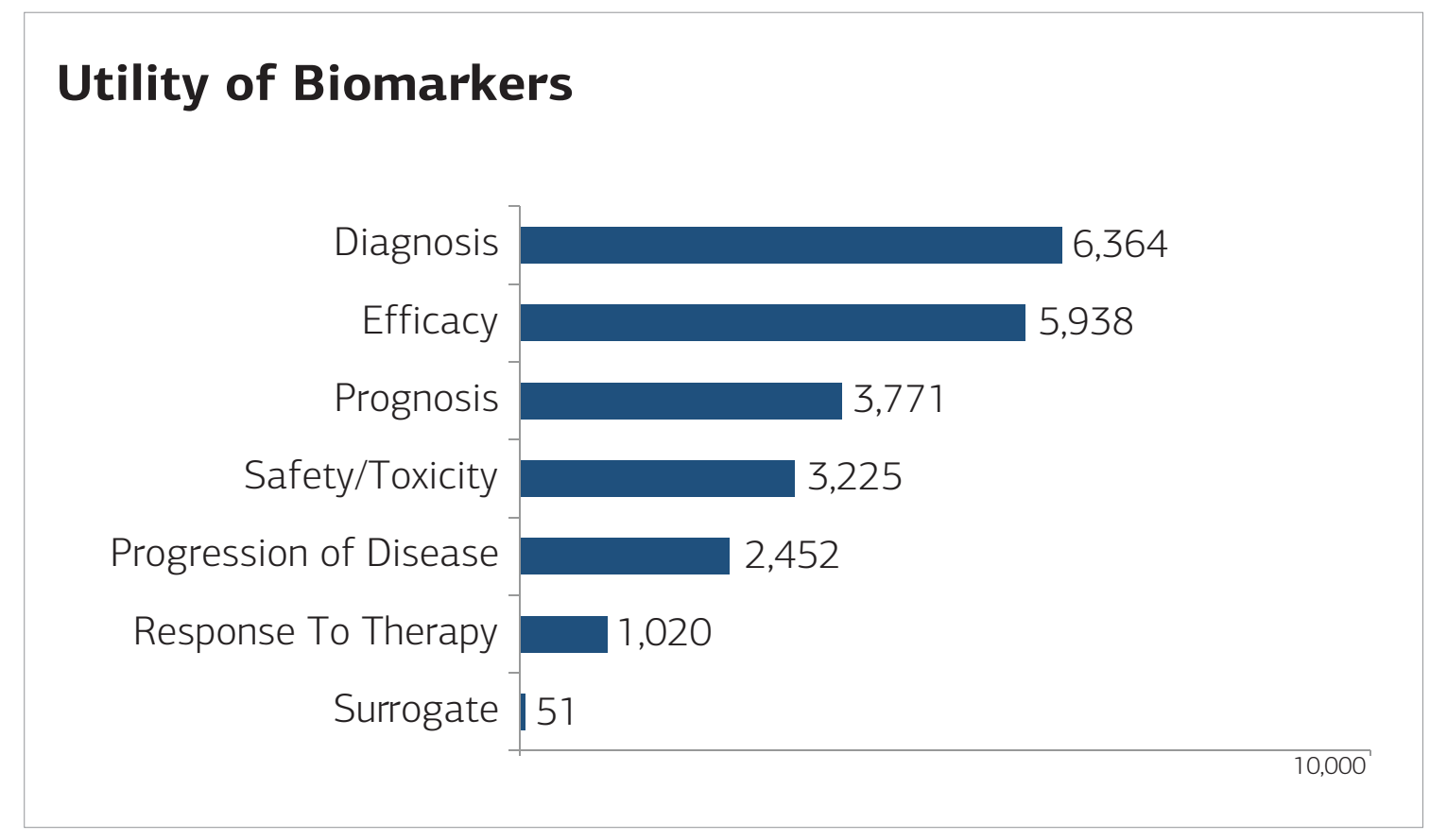
GOBIOM Statistics

Therapeutic Area	Number of Biomarkers	Number of Indications
Oncology	6335	123
Diseases of the circulatory system	1204	111
Endocrine, nutritional and metabolic diseases	932	78
Diseases of the musculoskeletal system and connective tissue	668	30
Mental and behavioral disorders	610	27
Diseases of the digestive system	563	37
Diseases of the nervous system	538	34
Infectious and parasitic diseases	421	28
Diseases of the genitourinary system	355	29
Diseases of the respiratory system	330	17
Injury, poisoning and certain other consequences of external causes	199	6
Diseases of the skin and subcutaneous tissue	118	12
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	68	9
Diseases of the eye and adnexa	35	8
Diseases of the ear and mastoid process	4	1
Others	897	1
Total :	**13277**	**551**

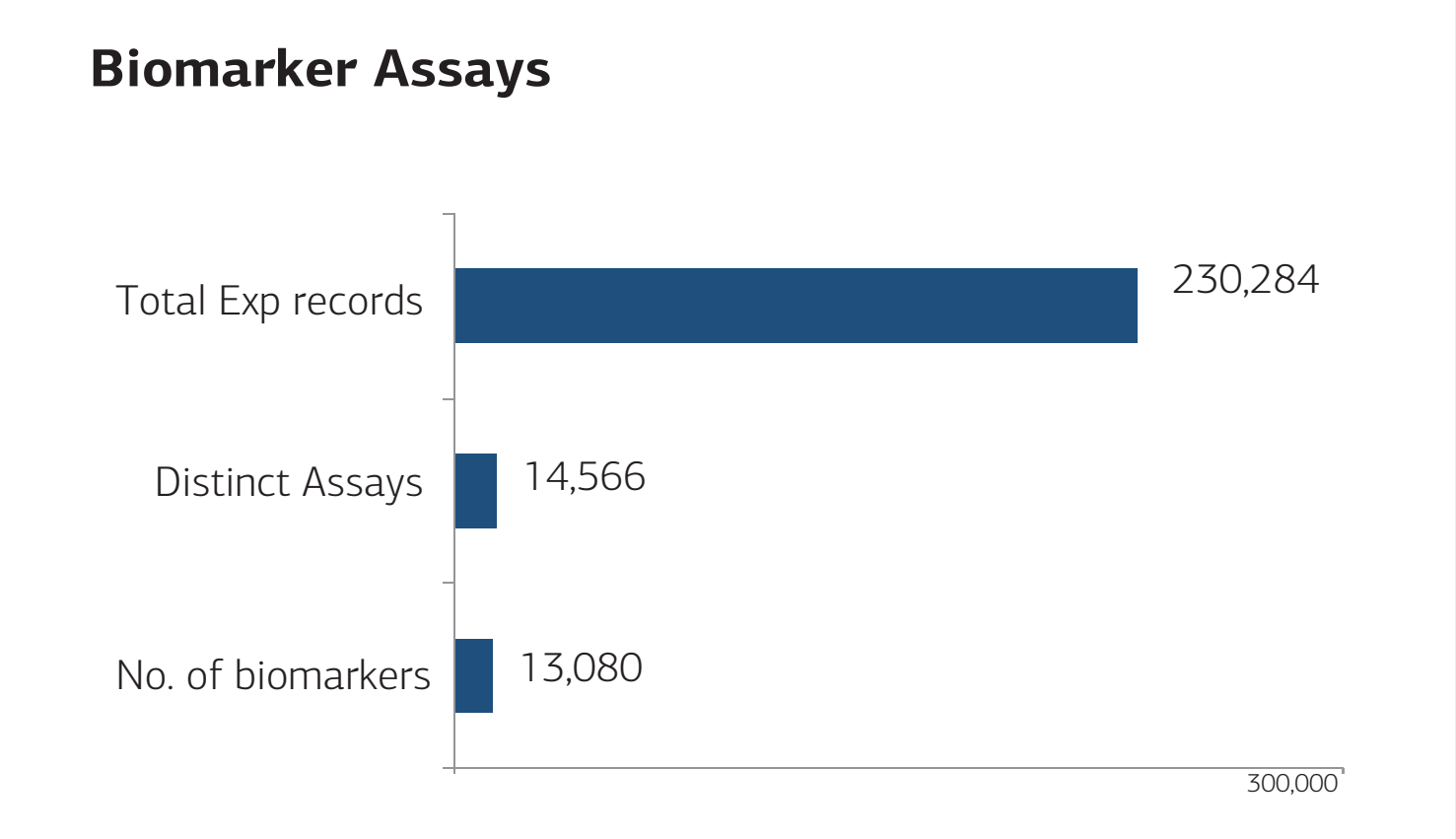
Types of Biomarkers



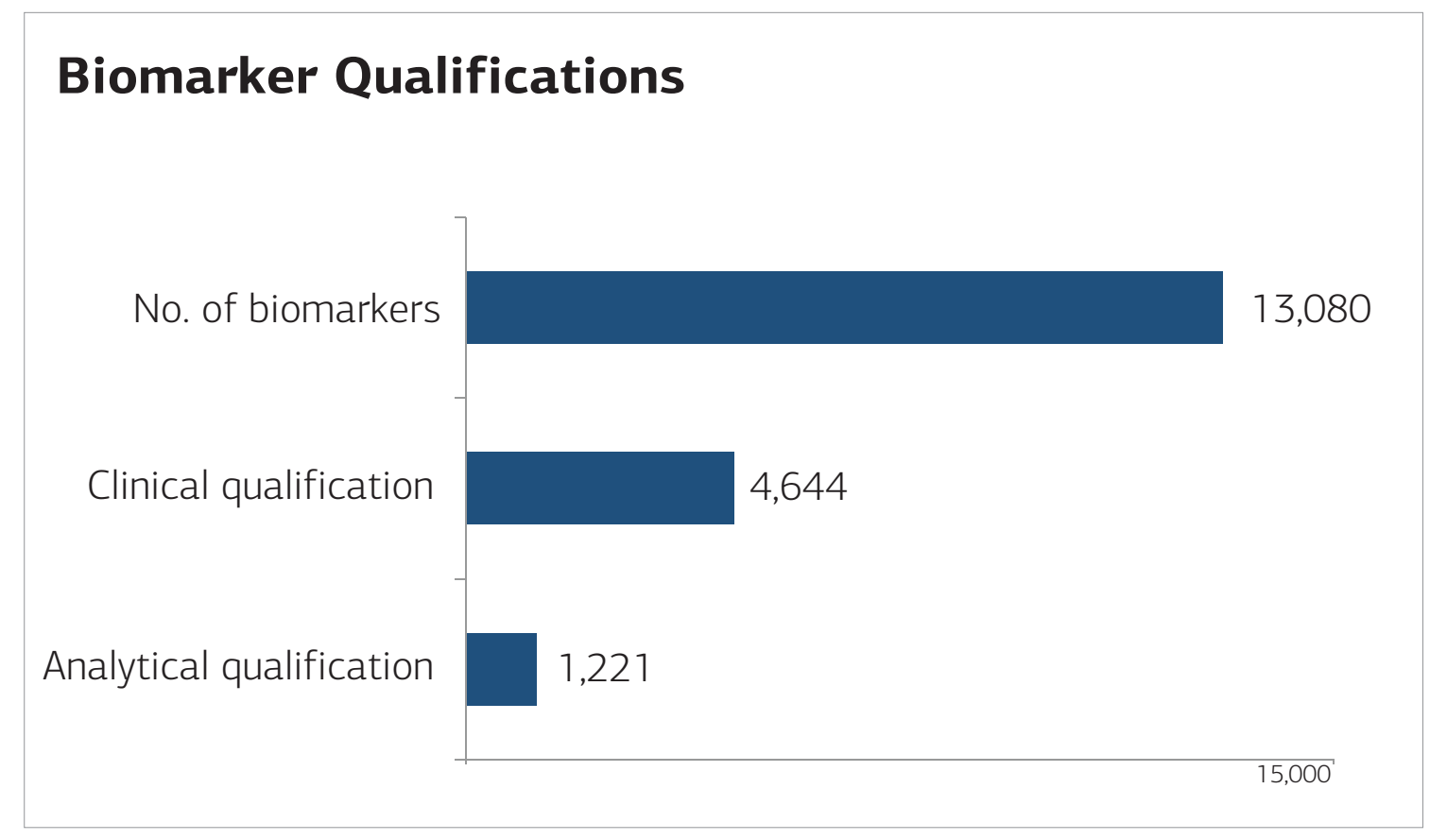
Utility of Biomarkers



Biomarker Assays

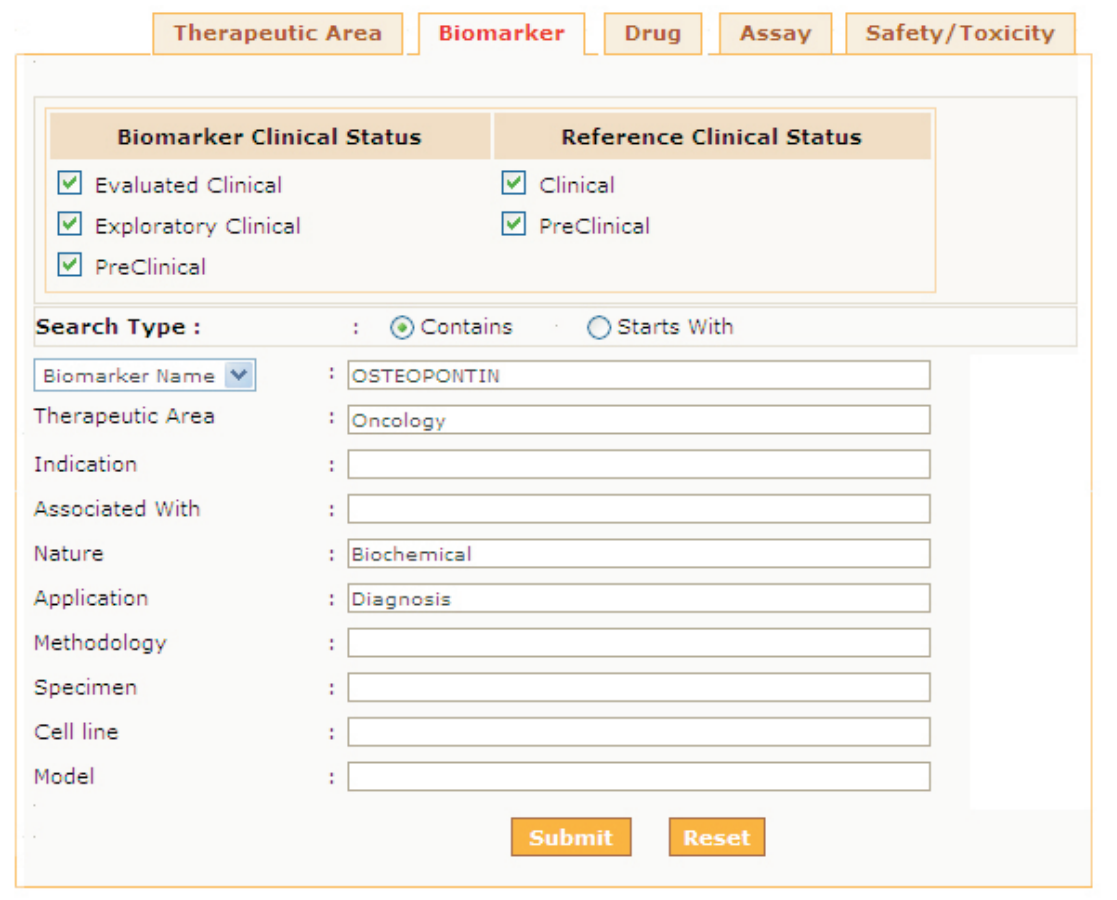


Biomarker Qualifications



Methodology

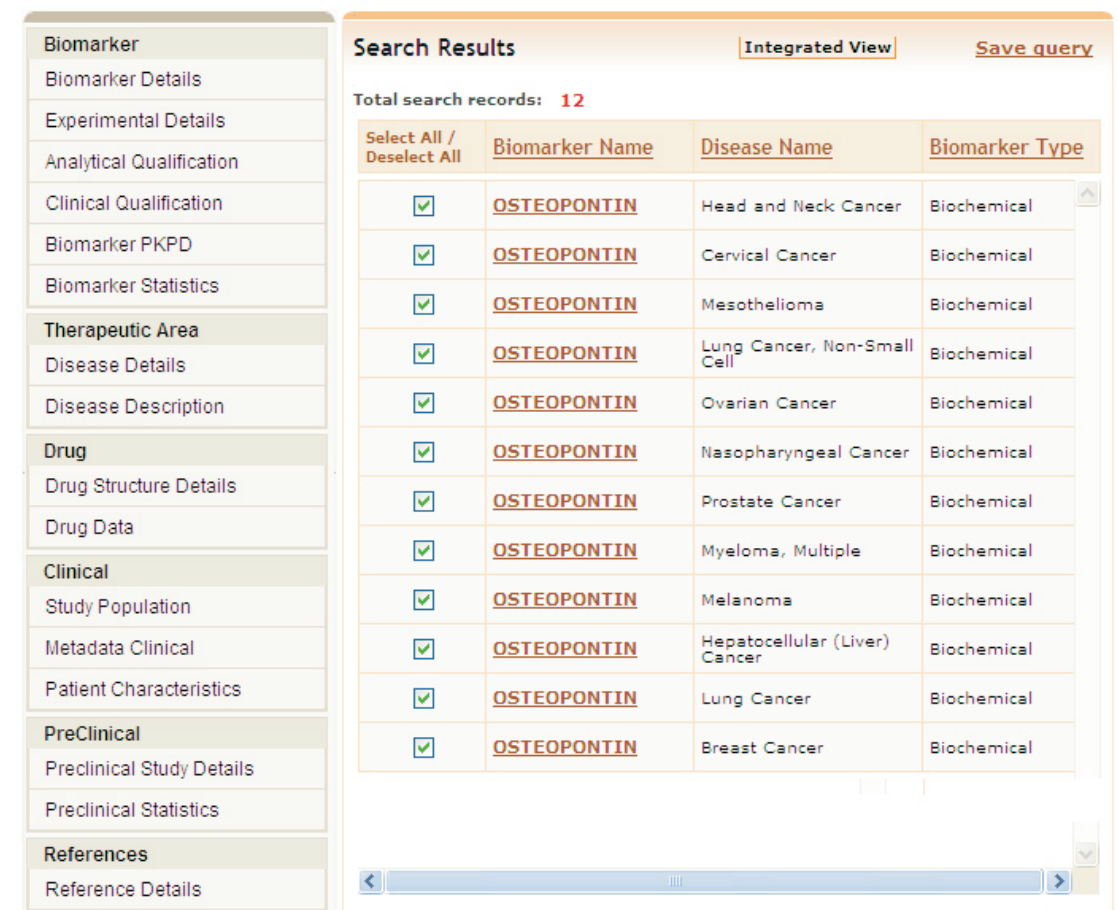
Identify the cancers for which Osteopontin is reported as a biochemical diagnostic marker in the published literature.



Biomarker Clinical Status	Reference Clinical Status
☑ Evaluated Clinical	☑ Clinical
☑ Exploratory Clinical	☑ PreClinical
☑ PreClinical	

Search Type : ● Contains ○ Starts With
Biomarker Name : OSTEOPONTIN
Therapeutic Area : Oncology
Indication :
Associated With :
Nature : Biochemical
Application : Diagnosis
Methodology :
Specimen :
Cell line :
Model :

Osteopontin is reported as a diagnostic marker for 12 oncology indications.

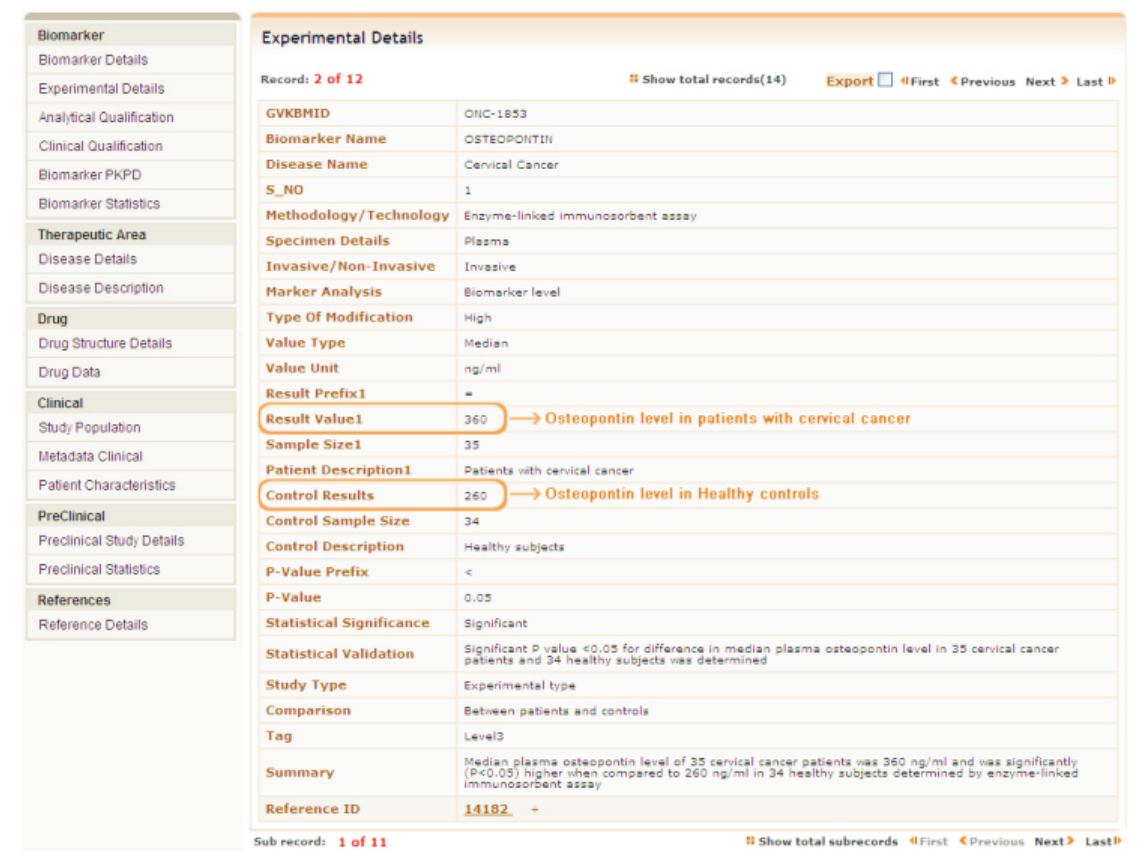


Search Results

Total search records: 12

Select All / Deselect All	Biomarker Name	Disease Name	Biomarker Type
☑	OSTEOPONTIN	Head and Neck Cancer	Biochemical
☑	OSTEOPONTIN	Cervical Cancer	Biochemical
☑	OSTEOPONTIN	Mesothelioma	Biochemical
☑	OSTEOPONTIN	Lung Cancer, Non-Small Cell	Biochemical
☑	OSTEOPONTIN	Ovarian Cancer	Biochemical
☑	OSTEOPONTIN	Nasopharyngeal Cancer	Biochemical
☑	OSTEOPONTIN	Prostate Cancer	Biochemical
☑	OSTEOPONTIN	Myeloma, Multiple	Biochemical
☑	OSTEOPONTIN	Melanoma	Biochemical
☑	OSTEOPONTIN	Hepatocellular (Liver) Cancer	Biochemical
☑	OSTEOPONTIN	Lung Cancer	Biochemical
☑	OSTEOPONTIN	Breast Cancer	Biochemical

Identify the variation in the Osteopontin level in disease condition compared to the healthy controls in all the reported indications.



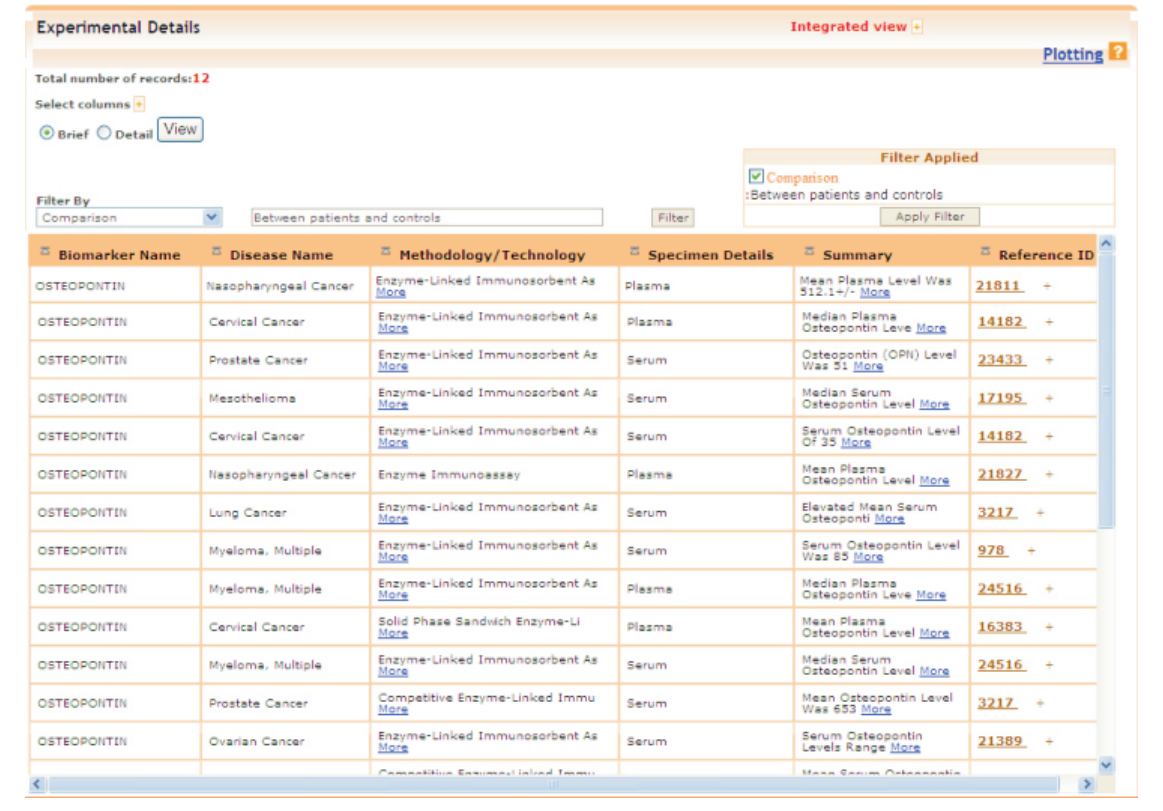
Experimental Details

Record: 2 of 12

GVKBMID	ONC-1853
Biomarker Name	OSTEOPONTIN
Disease Name	Cervical Cancer
S_NO	1
Methodology/Technology	Enzyme-linked immunosorbent assay
Specimen Details	Plasma
Invasive/Non-Invasive	Invasive
Marker Analysis	Biomarker level
Type Of Modification	High
Value Type	Median
Value Unit	ng/ml
Result Prefix1	=
Result Value1	360 → Osteopontin level in patients with cervical cancer
Sample Size1	35
Patient Description1	Patients with cervical cancer
Control Results	260 → Osteopontin level in Healthy controls
Control Sample Size	34
Control Description	Healthy subjects
P-Value Prefix	<
P-Value	0.05
Statistical Significance	Significant
Statistical Validation	Significant P value <0.05 for difference in median plasma osteopontin level in 35 cervical cancer patients and 34 healthy subjects was determined
Study Type	Experimental type
Comparison	Between patients and controls
Tag	Level3
Summary	Median plasma osteopontin level of 35 cervical cancer patients was 360 ng/ml and was significantly (P<0.05) higher when compared to 260 ng/ml in 34 healthy subjects determined by enzyme-linked immunosorbent assay
Reference ID	14182 +

Sub record: 1 of 11

To analyze the variation of osteopontin levels in different cancers simultaneously, select all the records and click on integrated view and Filter the datapoints which give information on the Osteopontin levels in diseased condition compared to healthy controls.



Experimental Details

Total number of records:12

Select columns

● Brief ○ Detail

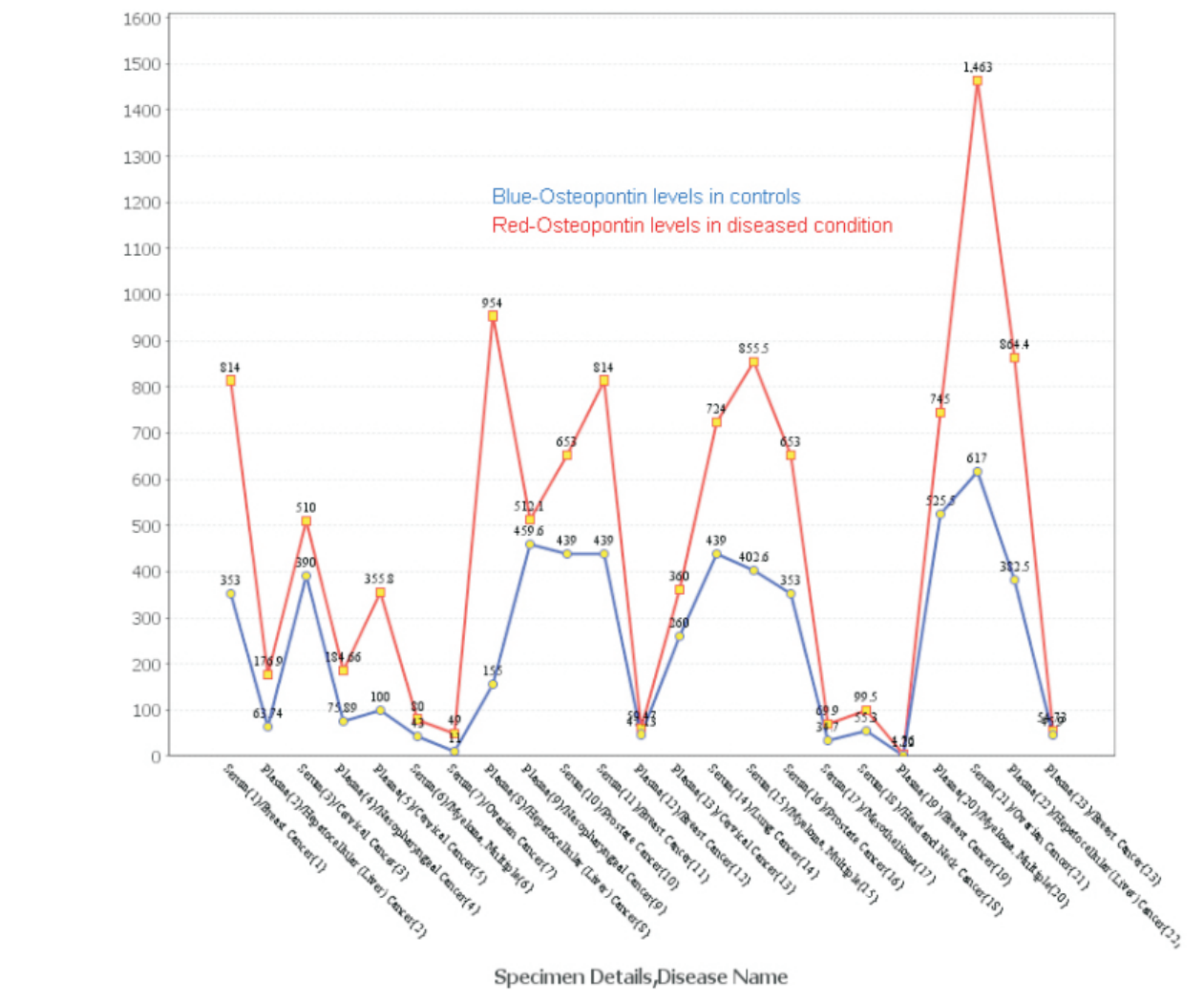
Filter By: Comparison — Between patients and controls

Filter Applied: ☑ Comparison :Between patients and controls

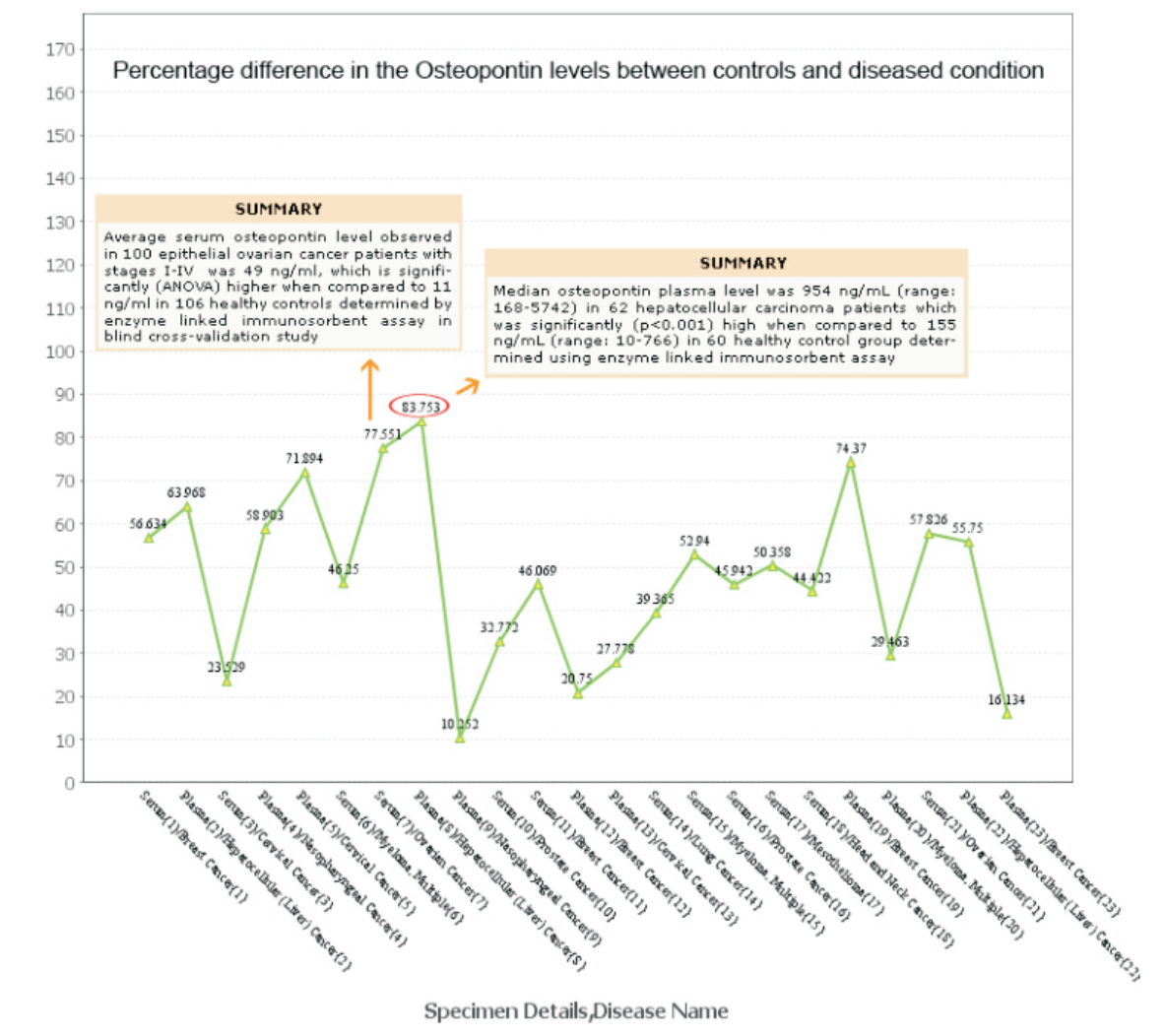
Biomarker Name	Disease Name	Methodology/Technology	Specimen Details	Summary	Reference ID
OSTEOPONTIN	Nasopharyngeal Cancer	Enzyme-Linked Immunosorbent As More	Plasma	Mean Plasma Level Was 512.1+/- More	21811 +
OSTEOPONTIN	Cervical Cancer	Enzyme-Linked Immunosorbent As More	Plasma	Median Plasma Osteopontin Leve More	14182 +
OSTEOPONTIN	Prostate Cancer	Enzyme-Linked Immunosorbent As More	Serum	Osteopontin (OPN) Level Was 51 More	23433 +
OSTEOPONTIN	Mesothelioma	Enzyme-Linked Immunosorbent As More	Serum	Median Serum Osteopontin Level More	17195 +
OSTEOPONTIN	Cervical Cancer	Enzyme-Linked Immunosorbent As More	Serum	Serum Osteopontin Level Of 35 More	14182 +
OSTEOPONTIN	Nasopharyngeal Cancer	Enzyme Immunoassay	Plasma	Mean Plasma Osteopontin Level More	21827 +
OSTEOPONTIN	Lung Cancer	Enzyme-Linked Immunosorbent As More	Serum	Elevated Mean Serum Osteoponti More	3217 +
OSTEOPONTIN	Myeloma, Multiple	Enzyme-Linked Immunosorbent As More	Serum	Serum Osteopontin Level Was 85 More	978 +
OSTEOPONTIN	Myeloma, Multiple	Enzyme-Linked Immunosorbent As More	Plasma	Median Plasma Osteopontin Leve More	24516 +
OSTEOPONTIN	Cervical Cancer	Solid Phase Sandwich Enzyme-Li More	Plasma	Mean Plasma Osteopontin Level More	16383 +
OSTEOPONTIN	Myeloma, Multiple	Enzyme-Linked Immunosorbent As More	Serum	Median Serum Osteopontin Level More	24516 +
OSTEOPONTIN	Prostate Cancer	Competitive Enzyme-Linked Immu More	Serum	Mean Osteopontin Level Was 653 More	3217 +
OSTEOPONTIN	Ovarian Cancer	Enzyme-Linked Immunosorbent As More	Serum	Serum Osteopontin Levels Range More	21389 +

Data Analysis

Plot the Osteopontin levels between the controls and the diseased condition using in-built analysis tools present in GOBIOM.



Plot the % difference in the Osteopontin levels.



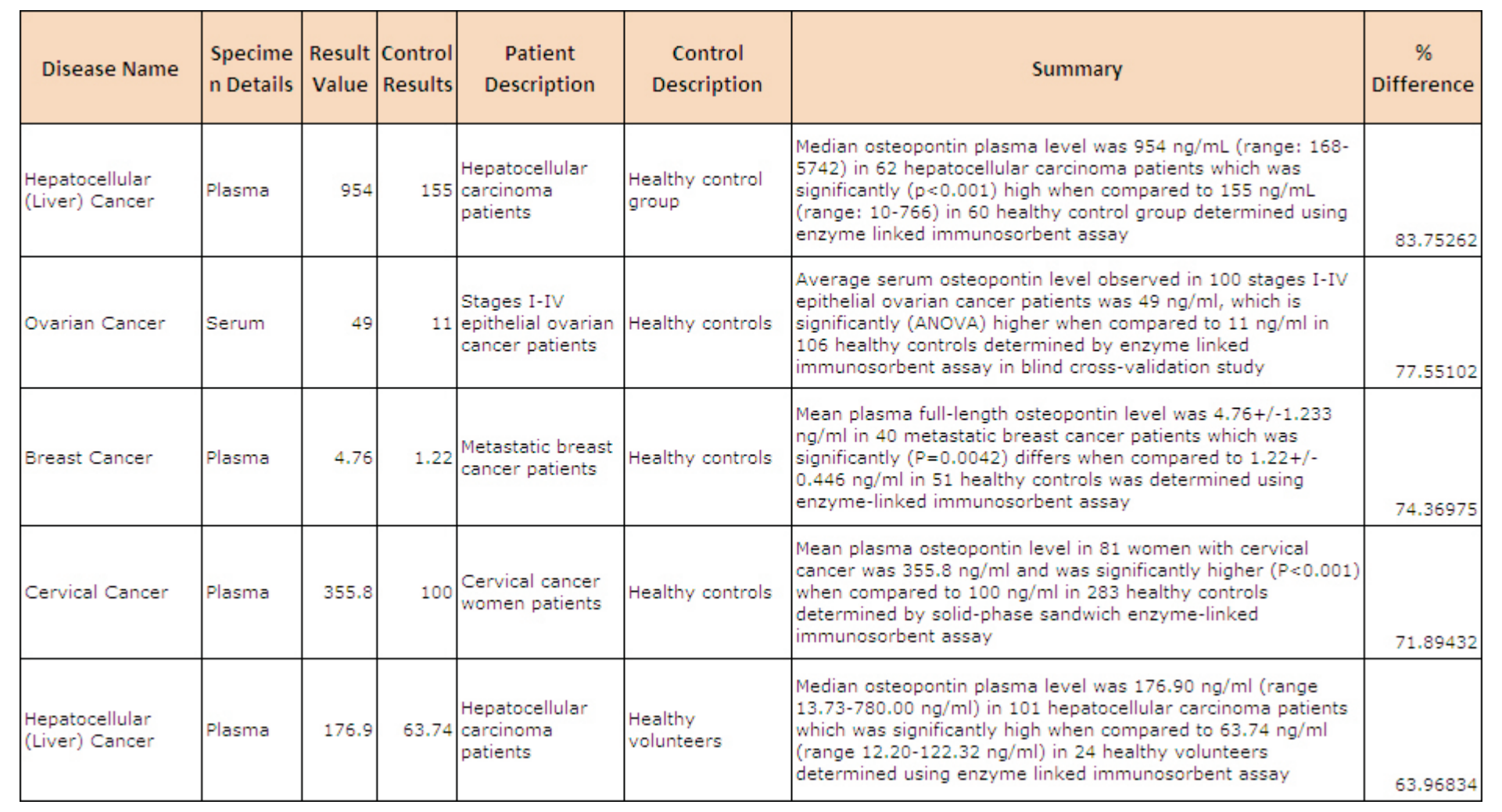
SUMMARY

Average serum osteopontin level observed in 100 epithelial ovarian cancer patients with stages I-IV was 49 ng/ml, which is significantly (ANOVA) higher when compared to 11 ng/ml in 106 healthy controls determined by enzyme linked immunosorbent assay in blind cross-validation study

SUMMARY

Median osteopontin plasma level was 954 ng/mL (range: 168-5742) in 62 hepatocellular carcinoma patients which was significantly (p<0.001) high when compared to 155 ng/mL (range: 10-766) in 60 healthy control group determined using enzyme linked immunosorbent assay

Snapshot of the data behind the plot.



Disease Name	Specimen Details	Result Value	Control Results	Patient Description	Control Description	Summary	% Difference
Hepatocellular (Liver) Cancer	Plasma	954	155	Hepatocellular carcinoma patients	Healthy control group	Median osteopontin plasma level was 954 ng/mL (range: 168-5742) in 62 hepatocellular carcinoma patients which was significantly (p<0.001) high when compared to 155 ng/mL (range: 10-766) in 60 healthy control group determined using enzyme linked immunosorbent assay	83.75262
Ovarian Cancer	Serum	49	11	Stages I-IV epithelial ovarian cancer patients	Healthy controls	Average serum osteopontin level observed in 100 stages I-IV epithelial ovarian cancer patients was 49 ng/ml, which is significantly (ANOVA) higher when compared to 11 ng/ml in 106 healthy controls determined by enzyme linked immunosorbent assay in blind cross-validation study	77.55102
Breast Cancer	Plasma	4.76	1.22	Metastatic breast cancer patients	Healthy controls	Mean plasma full-length osteopontin level was 4.76+/-1.233 ng/ml in 40 metastatic breast cancer patients which was significantly (P=0.0042) differs when compared to 1.22+/-0.446 ng/ml in 51 healthy controls was determined using enzyme-linked immunosorbent assay	74.36975
Cervical Cancer	Plasma	355.8	100	Cervical cancer women patients	Healthy controls	Mean plasma osteopontin level in 81 women with cervical cancer was 355.8 ng/ml and was significantly higher (P<0.001) when compared to 100 ng/ml in 283 healthy controls determined by solid-phase sandwich enzyme-linked immunosorbent assay	71.89432
Hepatocellular (Liver) Cancer	Plasma	176.9	63.74	Hepatocellular carcinoma patients	Healthy volunteers	Median osteopontin plasma level was 176.90 ng/ml (range 13.73-780.00 ng/ml) in 101 hepatocellular carcinoma patients which was significantly high when compared to 63.74 ng/ml (range 12.20-122.32 ng/ml) in 24 healthy volunteers determined using enzyme linked immunosorbent assay	63.96834

Conclusion

- Osteopontin is reported as a biochemical diagnostic marker for a variety of cancer
- By analyzing its levels in plasma or serum of diseased patients against healthy controls, it looks like OPN is a relatively good diagnostic marker of Hepatocellular cancer as there is highest variation of 83.7% compared to other cancers
- GOBIOM can be used rapidly and efficiently for any biomarker research analysis

Advantages of GOBIOM

- Over 350 datafields captured for every biomarker
- 551 therapeutic indications covered
- Controlled vocabulary through out the database
- Various parameters linking therapeutic interventions like dose, treatment duration, ethnicity and the relation between the biomarker and clinical outcome along with adverse effects are provided in a relational database which makes the end user to carry out easy biomarker analysis
- ~3000 drug-induced toxicity markers covering hepato, neuro, GI, nephro, cardio, endocrinal, vascular and other toxicities
- All the data points are linked to the valid references like pubmed, clinical trial registries or to the scientific conference website
- A user interface is designed to query the database either with biomarker name, indication, drug or the drug-induced organ disorder
- User can export the data to an excel file or XML or can generate a biomarker report in PDF format
- User can analyse the biomarker data using analysis tools linked to the UI
- Manual curation of the data with periodic updation
- Easy integration with client proprietary data
- Alert service on new marker addition or existing marker updation
- On-demand service for any biomarker addition into the database
- 'Alert a colleague' option to share the biomarker data between users
- Competitive intelligence analysis
- On-demand training sessions

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