OCA plus Scientific Network

Eloisa Jantus Lewintre[1], Ludovic Lacroix[2], Karl Kashofer[3], Tom van Wezel[4], Massimo Barberis[5]

[1] Fundacion Investigacion GVA, Valencia, Spain
[2] Institute Gustave Roussy, Paris, France
[3] Medical University of Graz, Graz, Austria
[4] Leiden University Medical Center, Leiden, The Netherlands
[5] Istituto Europeo di Oncologia, Milano, Italy






Disclosures

- Thermo Fisher Scientific and its affiliates are not endorsing, recommending or promoting any use or application of Thermo Fisher Scientific products by third parties during this seminar.
- Information and materials presented or provided by third parties as-is and without warranty of any kind, including regarding intellectual property rights and reported results.
- Parties presenting images, text and material represent they have the right to do so.
- Speaker is provided honorarium for this presentation.

Disclosures

- Advisory fee/honoraria: Roche, MSD, BMS, Pfizer, Astra Zeneca, Amgen, Thermo Fisher Scientific, Illumina, Biocartis

The implementation of genomics-driven cancer medicine, including the technical infrastructure required and challenges faced, have been well described, confirming broad implementation of NGS testing in a clinical setting is feasible

VOLUME 33 · NUMBER 25 · SEPTEMBER 1 2015

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Feasibility of Large-Scale Genomic Testing to Facilitate Enrollment Onto Genomically Matched Clinical Trials

Funda Meric-Bernstam, Lauren Brusco, Kenna Shaw, Chacha Horombe, Scott Kopetz, Michael A. Davies, Mark Routbort, Sarina A. Piha-Paul, Filip Janku, Naoto Ueno, David Hong, John De Groot, Vinod Ravi, Yisheng Li, Raja Luthra, Keyur Patel, Russell Broaddus, John Mendelsohn, and Gordon B. Mills

Comprehensive genomic profiling (CGP) is a next-generation sequencing (NGS) approach that uses a single assay to assess hundreds of genes including relevant cancer biomarkers, as established in guidelines and clinical trials, for therapy guidance.

TMB
MSI

Published OnlineFirst May 18, 2016; DOI: 10.1158/0008-5472.CAN-15-3043

Clinical Studies

Cancer Research

Cancer Therapy Directed by Comprehensive Genomic Profiling: A Single Center Study

Jennifer J. Wheler[1], Filip Janku[1], Aung Naing[1], Yali Li[2], Bettzy Stephen[1], Ralph Zinner[1], Vivek Subbiah[1], Siqing Fu[1], Daniel Karp[1], Gerald S. Falchook[3], Apostolia M. Tsimberidou[1], Sarina Piha-Paul[1], Roosevelt Anderson[1], Danxia Ke[1], Vincent Miller[2], Roman Yelensky[2], J. Jack Lee[4], David S. Hong[1], and Razelle Kurzrock[5]

HHS Public Access

Author manuscript

Nat Med. Author manuscript; available in PMC 2017 November 08.

Published in final edited form as:

Nat Med. 2017 June ; 23(6): 703–713. doi:10.1038/nm.4333.

Mutational Landscape of Metastatic Cancer Revealed from Prospective Clinical Sequencing of 10,000 Patients

The Oncologist®

Lung Cancer

Comprehensive Genomic Profiling Facilitates Implementation of the National Comprehensive Cancer Network Guidelines for Lung Cancer Biomarker Testing and Identifies Patients Who May Benefit From Enrollment in Mechanism-Driven Clinical Trials

James H. Suh,[a] Adrienne Johnson,[a] Lee Albacker,[a] Kai Wang,[a,b] Juliann Chmielecki,[a] Garrett Frampton,[a] Laurie Gay,[a] Julia A. Elvin,[a] Jo-Anne Vergilio,[a] Siraj Ali,[a] Vincent A. Miller,[a] Philip J. Stephens,[a] Jeffrey S. Ross[a]

[a]Foundation Medicine, Inc., Cambridge, Massachusetts, USA; [b]Zhejiang Cancer Hospital, Hangzhou, People's Republic of China

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Non-small cell lung cancer • Comprehensive genomic profiling • National Comprehensive Cancer Network guidelines • Clinical trials

The Oncologist®

Cancer Diagnostics and Molecular Pathology

Clinical Actionability of Comprehensive Genomic Profiling for Management of Rare or Refractory Cancers

Kim M. Hirshfield,[a] Denis Tolkunov,[b] Hua Zhong,[c] Siraj M. Ali,[h] Mark N. Stein,[a] Susan Murphy,[d] Hetal Vig,[a] Alexei Vazquez,[e] John Glod,[d] Rebecca A. Moss,[a] Vladimir Belyi,[b] Chang S. Chan,[a] Suzie Chen,[i] Lauri Goodell,[c] David Foran,[c] Roman Yelensky,[h] Norma A. Palma,[h] James X. Sun,[h] Vincent A. Miller,[h] Philip J. Stephens,[h] Jeffrey S. Ross,[h,j] Howard Kaufman,[f] Elizabeth Poplin,[a] Janice Mehnert,[a] Antoinette R. Tan,[a] Joseph R. Bertino,[a] Joseph Aisner,[a] Robert S. DiPaola,[a] Lorna Rodriguez-Rodriguez,[g] Shridar Ganesan[a]

[a]Division of Medical Oncology, Department of Medicine, [b]Department of Clinical Informatics, [c]Department of Pathology and Laboratory Medicine, [d]Department of Pediatrics, [e]Department of Radiation Oncology, [f]Division of Surgical Oncology, Department of Surgery, and [g]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Rutgers Cancer Institute of New Jersey/Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, USA; [h]Foundation Medicine, Cambridge, Massachusetts, USA; [i]Department of Chemical Biology, Rutgers, The State University of New Jersey, New Brunswick, New Jersey, USA; [j]Department of Pathology and Laboratory Medicine, Albany Medical College, Albany, New York, USA

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Molecular sequencing • Cancer • Tumor genomics • Molecular targeted therapy • Mutation

RESEARCH

Effect of a Collaboration Between a Health Plan, Oncology Practice, and Comprehensive Genomic Profiling Company from the Payer Perspective

Mitchell Reitsma, BA, MBA; John Fox, MD; Pierre Vanden Borre, PhD; Matthew Cavanaugh, BSN, RN; Yakov Chudnovsky, PhD; Rachel L. Erlich, PhD; Thomas E. Gribbin, MD; and Rachel Anhorn, PharmD

original report

Use of a Targeted Exome Next-Generation Sequencing Panel Offers Therapeutic Opportunity and Clinical Benefit in a Subset of Patients With Advanced Cancers

Scott Kopetz, MD, PhD[1]; Kenna R. Mills Shaw, PhD[1]; J. Jack Lee, MD[1]; Jiexin Zhang, MS[1]; Beate Litzenburger, PhD[1]; Vijaykumar Holla, PhD[1]; Walter Kinyua, MS[1]; Emily Broaddus[1]; Molly S. Daniels, MS[1]; Funda Meric-Bernstam, MD, PhD[1]; and Russell R. Broaddus, MD, PhD[1]

Centralized/outsourcing vs in house

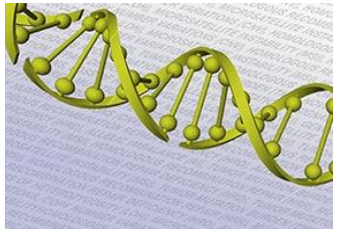
Centralized/outsourcing

In house

Comprehensive genomic profiling to detect different biomarkers sparing precious samples to obtain a single report.

Oncomine Comprehensive Assay Plus

Oncomine Comprehensive Assay Plus



- Profile 500+ unique genes
- SNVs, indels, CNVs, known and novel fusions, and splice variants
- Tumor mutational burden (TMB) microsatellite instability (MSI)
- Variants in 42 HRR pathway genes and genomic instability with loss of heterozygosity (LOH)
- Highly automated workflow and streamlined bioinformatics analysis

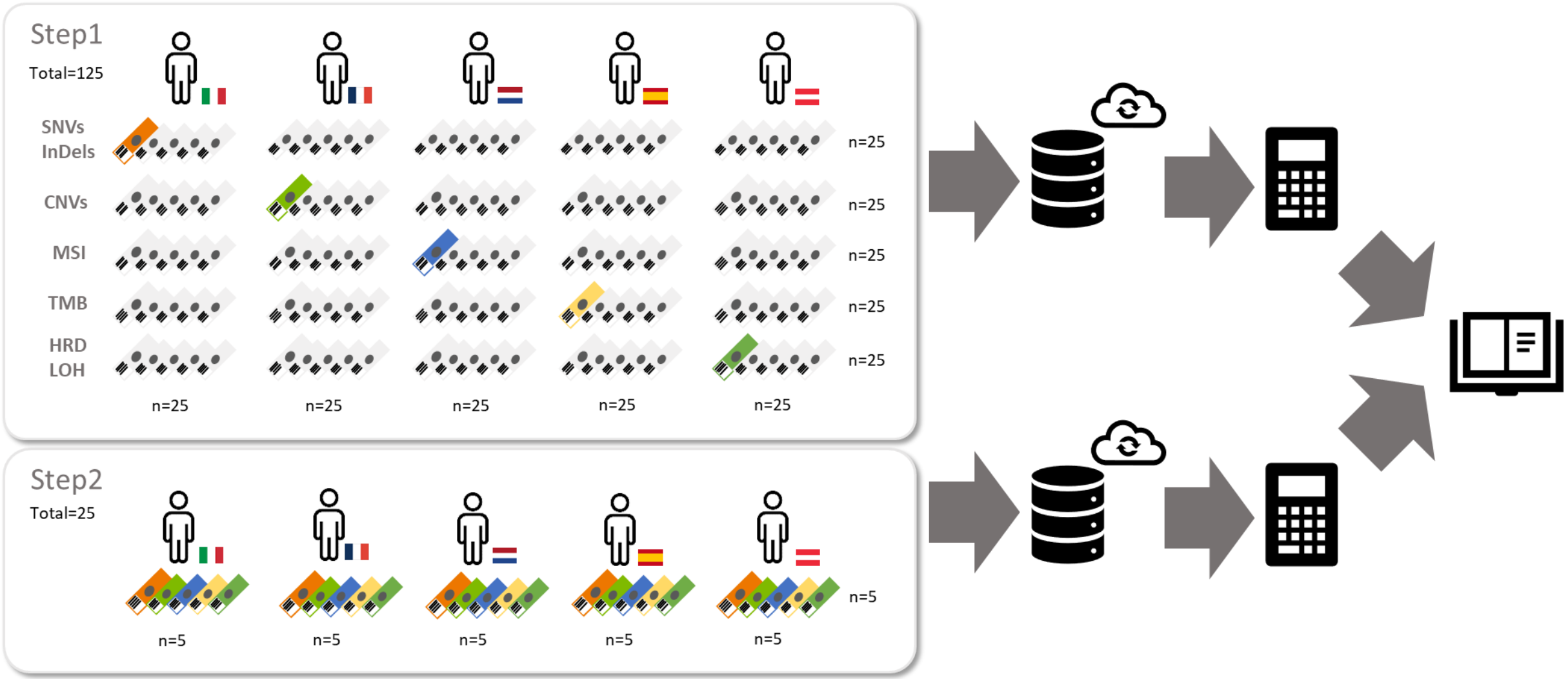
OCA Plus Network – Overall Strategy and Structure

n=5 centres with OCA Plus capability

Performance validation :
1.SNVs/InDels
2.CNVs
3.MSI
4.HRD/LOH
5.TMB

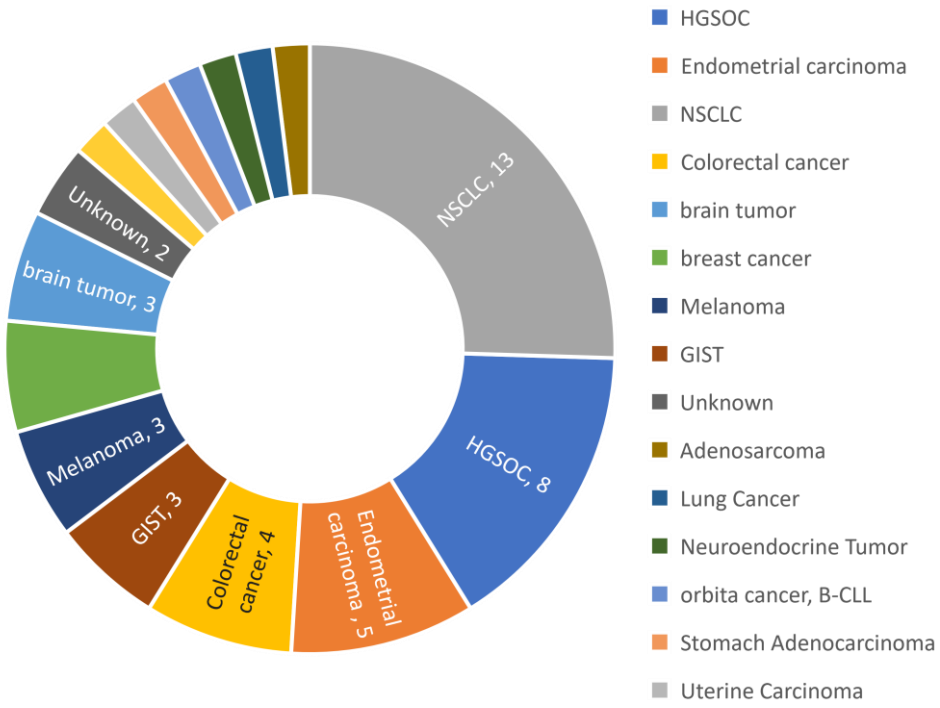
Clinical Applicably: FFPE resections, solid tumors

OCA Plus Network – Study design

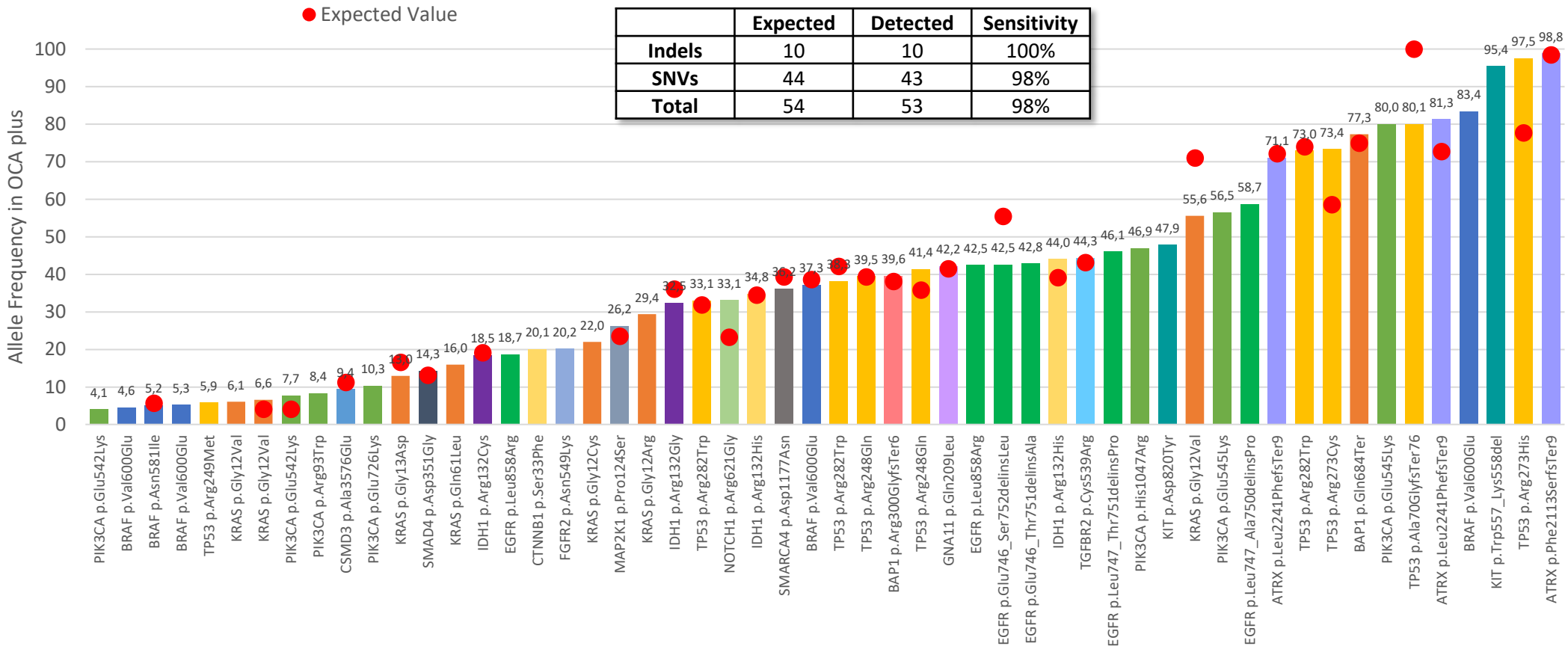


Project status summary and examples

- Out of targeted 125 clinical FFPE samples, the analysis of 51 samples have been completed so far.
- Analysed samples represent various cancer types, majority of which are NSCLC, Ovarian, Colon, GIST, Melanoma and Breast Cancer.
- 2 samples were discarded due to low uniformity.
- Samples have been pre-characterized with diverse methods on specific end-point (ex: NGS, low density WGS, MSI, FISH, RT-PCR, MLPA, etc)



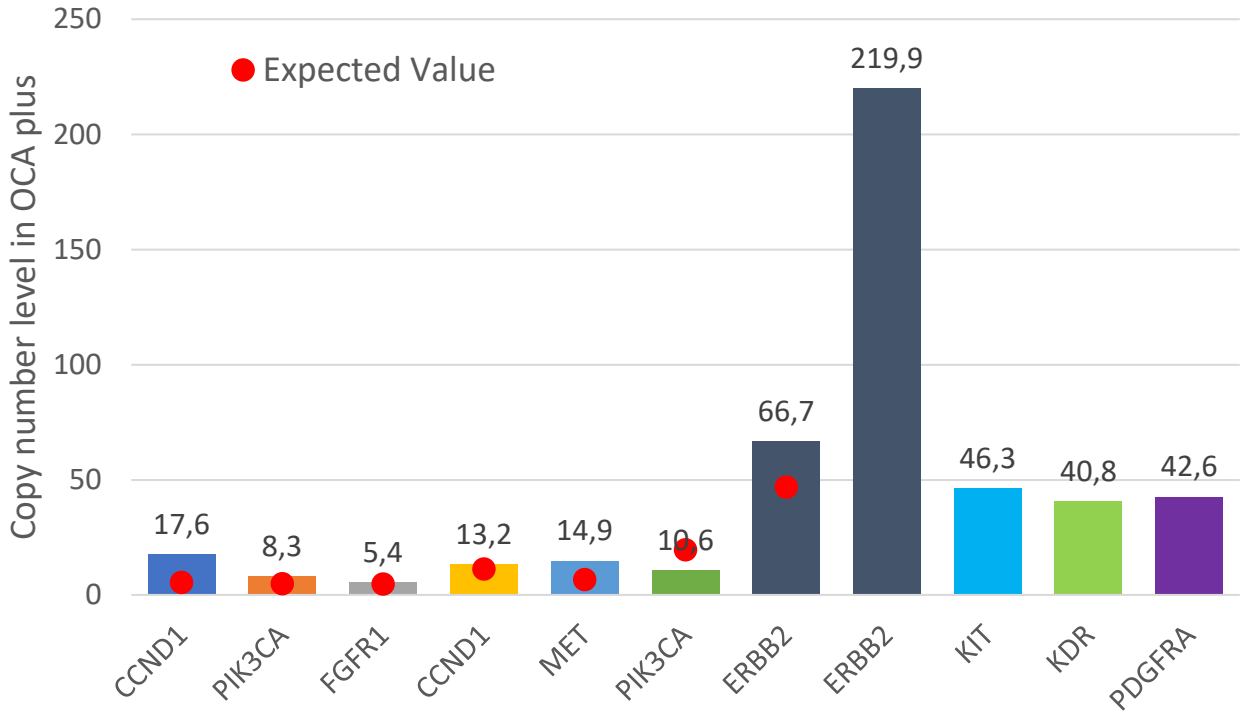
SNVs and InDels evaluated using OCA plus



	Expected	Detected	Sensitivity
Indels	10	10	100%
SNVs	44	43	98%
Total	54	53	98%

- Oncomine Comprehensive Assay plus detected with high sensitivity expected SNVs and InDels
- Allelic fractions detected were similar to the expected value

Copy Number Variants evaluated using OCA plus



- Oncomine Comprehensive Assay plus verified with high sensitivity expected CNVs
- Samples were pre-characterized using different methodologies including NGS, FISH and IHC

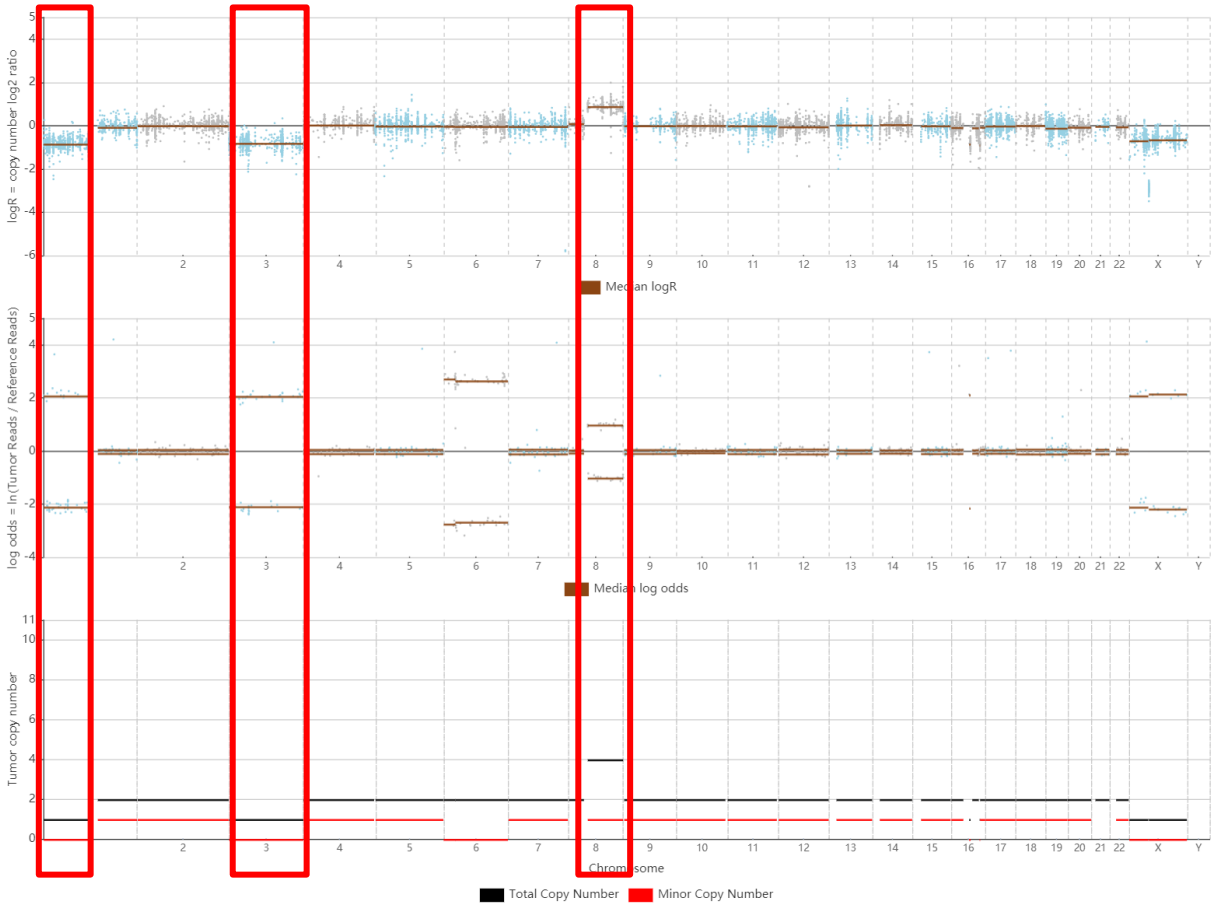
Chromosomal Level CNV evaluation using OCA plus

Oncomine Comprehensive plus standard result

Low-density WGS		OCA plus		Confirmed
region	status	cytoband	copy number	
1p	loss	1p36.33p12	x1	✓
3p	loss	3p26.3p12.1	x1	✓
3q	loss	3q11.1q29	x1	✓
8q	gain	8q11.22q24.3	x4	✓

- Melanoma sample characterized with low-density WGS
- Oncomine Comprehensive Assay plus verified all chromosomal alterations adding detailed cytoband coordinates
- The analysis view with genomic segmentation analysis can aid on advanced research analysis

Oncomine Comprehensive plus genomic segmentation



Microsatellite instability (MSI) evaluation using OCA plus

Oncomine Comprehensive plus standard result

Sample type	RT-PCR result	OCA plus		Concordance
		Status	Score	
Colorectal cancer	MSI-High	MSI-High	65.67	✓
Endometrial cancer	MSI-High	MSI-High	82.89	✓
Gastric cancer	MSI-High	MSI-High	219.61	✓

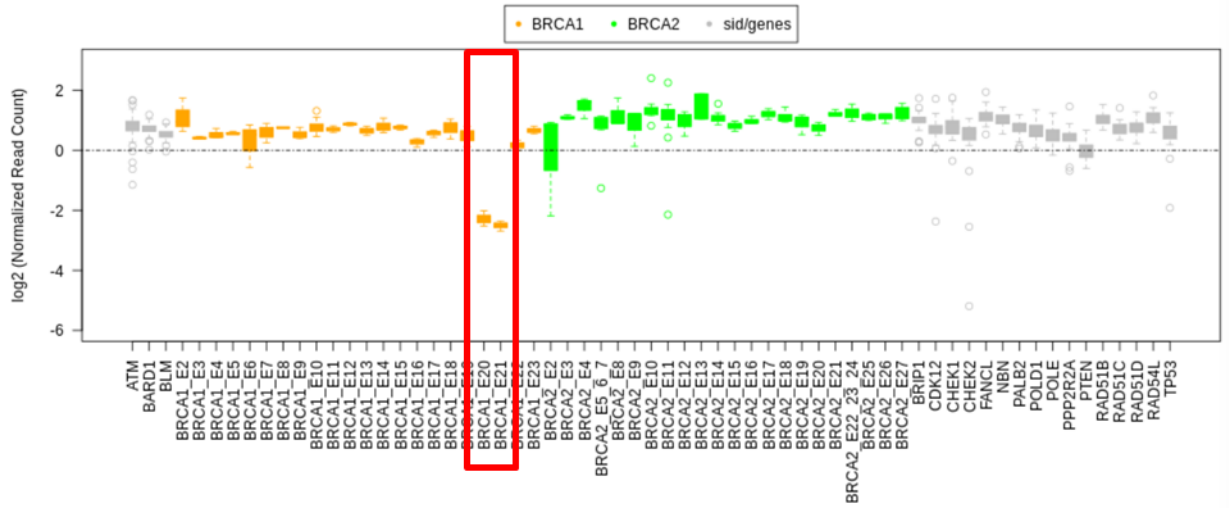
- Oncomine Comprehensive Assay plus verified the MSI-High status
- The analysis setting with mutational signatures can aid on advanced research analysis

Oncomine Comprehensive plus mutational signature

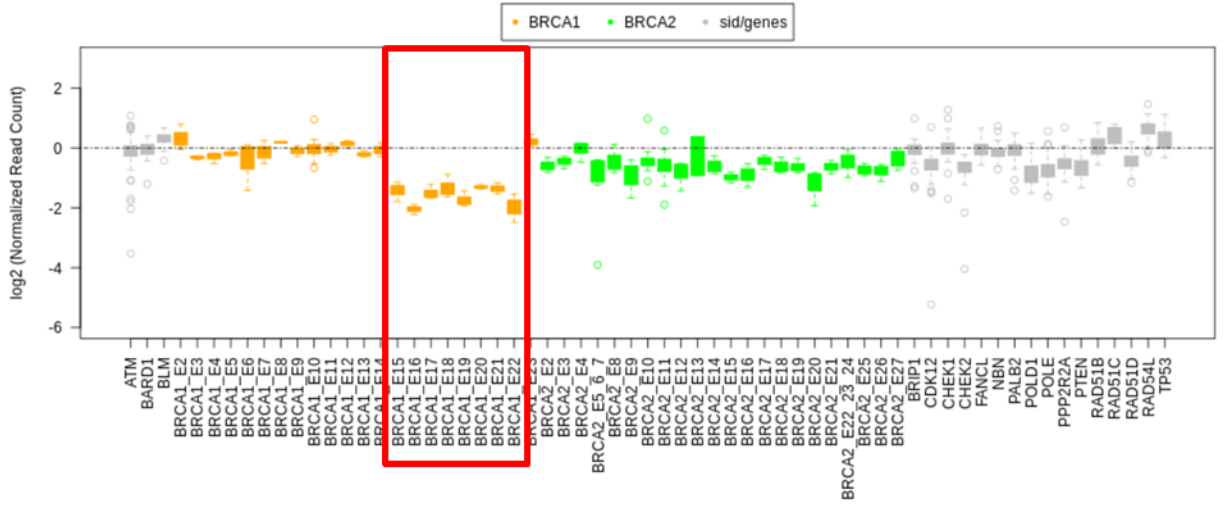
*SBS44 is mutational signature associated with DNA mismatch repair (microsatellite instability).

BRCA Exon Level Alterations using OCA plus

Ovarian cancer research sample with *BRCA1* Exon 20-21 deletion



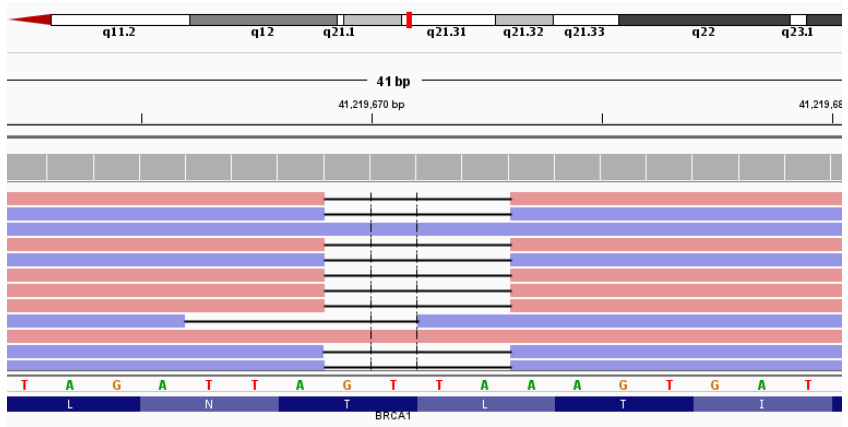
Ovarian cancer research sample with *BRCA1* Exon 15-22 deletion



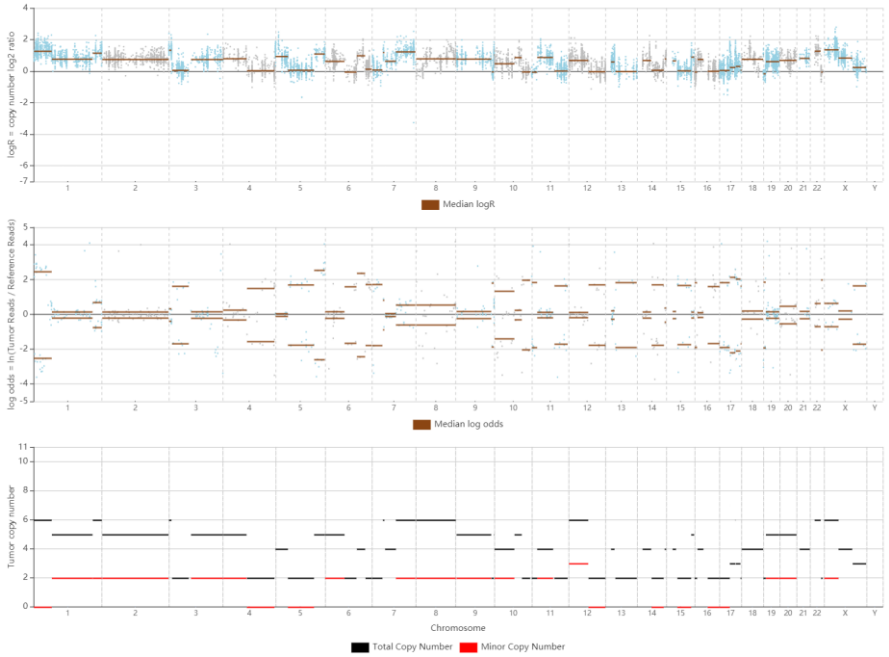
- Both research samples previously evaluated with MLPA
- Oncomine Comprehensive Assay plus verified the exon level alterations

Homologous Recombination Deficiency

- HGSOC sample with BRCA1 p.Thr1677IlefsTer2 mutation detected with OCAplus resulting in 38.99% LoH score.



- HGSOC sample had resulted in 34.9% LoH score with alternative method, confirmed with OCAplus resulting in 26.85% LoH Score. The patient received PARP inhibitors.



Conclusions

Oncomine Comprehensive Assay Plus is a true CGP:

It can detect biomarkers at nucleotide-level resolution and typically comprises all major genomic variant classes (SNVs, indels, CNVs, fusions, splice variants), as well as large genomic signatures (TMB, MSI), maximizing the ability to find clinically actionable alterations.

Oncomine Comprehensive Assay Plus is thought and produced to be an in-house testing

All the pathology assays from H&E stain to IHC and complex molecular assays can be done in our Labs.
We can achieve a patient-centered system keeping molecular profiling in house.
We can decide on the test flexibility based on the amount of sample available

Is sending samples to commercial laboratories abroad an ethical issue?

In many European countries the healthcare system is over 90% publicly financed. If we spend this money outside the system we do not support it and not enable its development

Thank You

IEO
European Institute of Oncology

Histopathology and Molecular Diagnostics Unit

Alessandra Rappa
Elena Guerini Rocco
Caterina Fumagalli
Paolo Lopedote
Alberto Ranghiero
Mila Schiavi
Tania Tamagni
Davide Vacirca