IBM Watson Health
Oncology and Genomics

Watson for Genomics

VII Simpósio Internacional de Câncer de Pulmão
Março 2019

IBM Watson Health™

Staying up-to-date with genomic information needs a new approach

3 million
Average number of publications related to cancer [1]

9 times
NCCN Guidelines changed for NSCLC in 2017 [2]

117
FDA approved biomarker-based drugs for cancer [3]

~50%
Of new FDA-approved cancer therapies (2016-17) require specific molecular features [5]

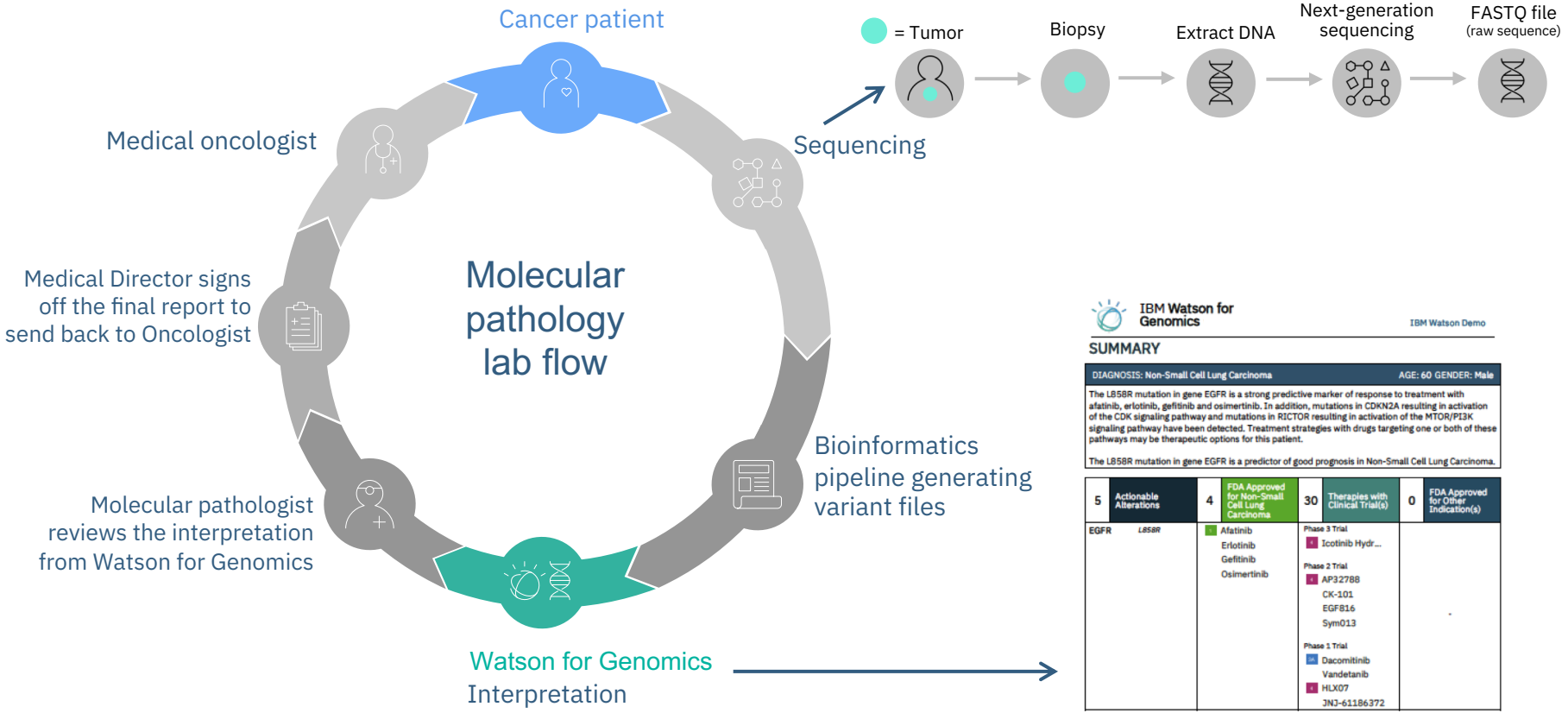
600%
Increase in % of US pts w/ cancer in 2018 est. to benefit from genome-targeted therapy from 2006 [6]

87%
Of Pharma pipe is biomarker driven drugs targeting late-stage cancer [4]

25%
The percent of variants of uncertain significance (VUS) that were reclassified [7]

1. Reyes-Aldasoro CC. The proportion of cancer-related entries in PubMed has increased considerably; is cancer truly "The Emperor of All Maladies"? Novelli G, ed. *PLoS ONE*. 2017;12(3):e0173671. doi:10.1371/journal.pone.0173671.
2. http://www.lungcancernews.org/2018/06/04/nccn-guidelines-updated-for-2018-keeping-pace-with-data/, Accessed August 9th, 2018
3. Julianne D. Twomey, Nina N. Brahme, Baolin Zhang,Drug-biomarker co-development in oncology – 20 years and counting,Drug Resistance Updates,Volume 30,2017,Pages 48-62, https://doi.org/10.1016/j.drup.2017.02.002.
4. Aitken, M., Kleinrock, M. & Kumar, S. *Global Oncology Trends 2017*. (IQVIA, 2017).
5. Heymach, J. *et al. J. Clin. Oncol.* **36**, 1020–1044 (2018).
6. Marquart J, Chen EY, Prasad V. Estimation of the Percentage of US Patients With Cancer Who Benefit From Genome-Driven Oncology. *JAMA Oncol.* 2018;4(8):1093–1098. doi:10.1001/jamaoncol.2018.1660
7. *JAMA.* 2018;320(12):1266-1274. doi:10.1001/jama.2018.13152

Where does Watson for Genomics fit in a lab workflow



Key features of Watson for Genomics

Comprehensive

Rely on expertly curated, clinical content based on the latest therapeutic options approved including targeted and immunotherapy options, professional guidelines, clinical trial options and relevant publications.

Fast

Save time and help reduce variability across reports with rapid, consistent, efficient and reproducible interpretation across cancer types.

Scalable

Easily scale sample volume and complexity of gene panel – from targeted panels to whole genome.

Evidence-based reporting

Depend on a clearly defined, level-of-evidence model, including pre-clinical information.

Saas service

Get started easily.
No hardware to purchase.
Minimal configuration required for initial use.

Security & privacy-compliant

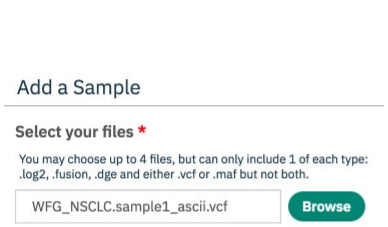
Designed to comply with HIPAA and GDPR requirements.

Watson for Genomics system overview

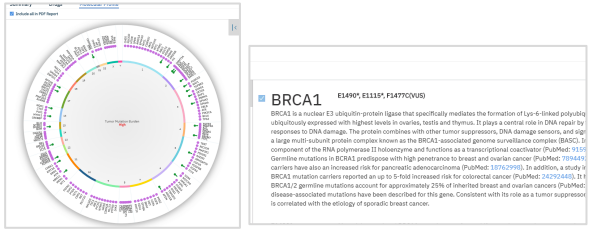
Add Sample
.vcf / .maf, .log2, .dge, .fusion

Watson for Genomics

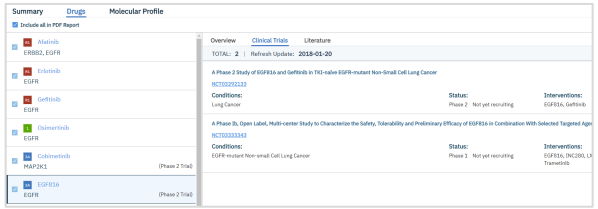
Report



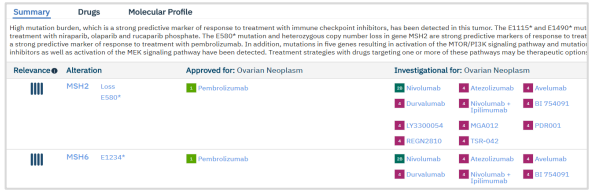
Molecular profile analysis

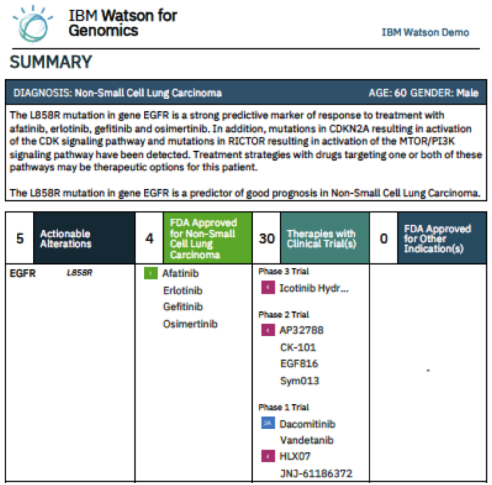


Drug analysis



Summary





Watson for Genomics reports on actionable mutations, therapeutic options and clinical trials within minutes

1. Automated case summary based on molecular profile
2. Automated classification of all genetic alterations
3. Clearly defined level of evidence model
4. Biomarker based clinical trial association
5. Speed and efficiency

- Display variant icons for the following types of mutation:

D Diagnostic mutation: a genetic alteration associated with a specific cancer type

P Cancer predisposing mutation: a genetic alteration associated with increased risk of cancer

R Resistance mutation: a genetic alteration predictive of lack of response to a given therapy

Px Prognostic mutation: a genetic alteration predictive of the likely course of the disease

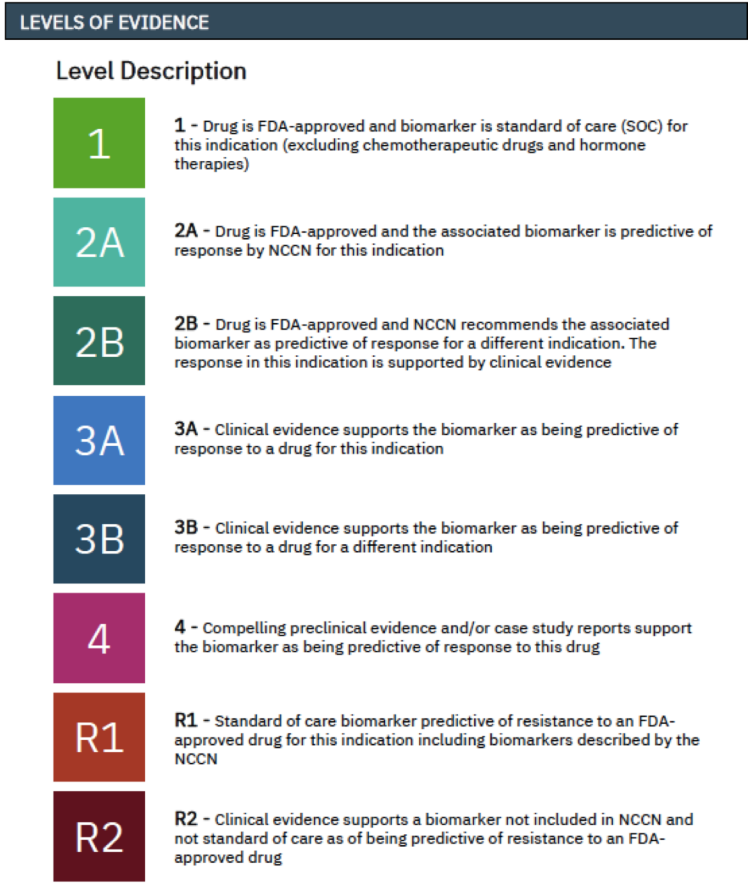
G Germline mutation: a hereditary genetic alteration

Level of evidence

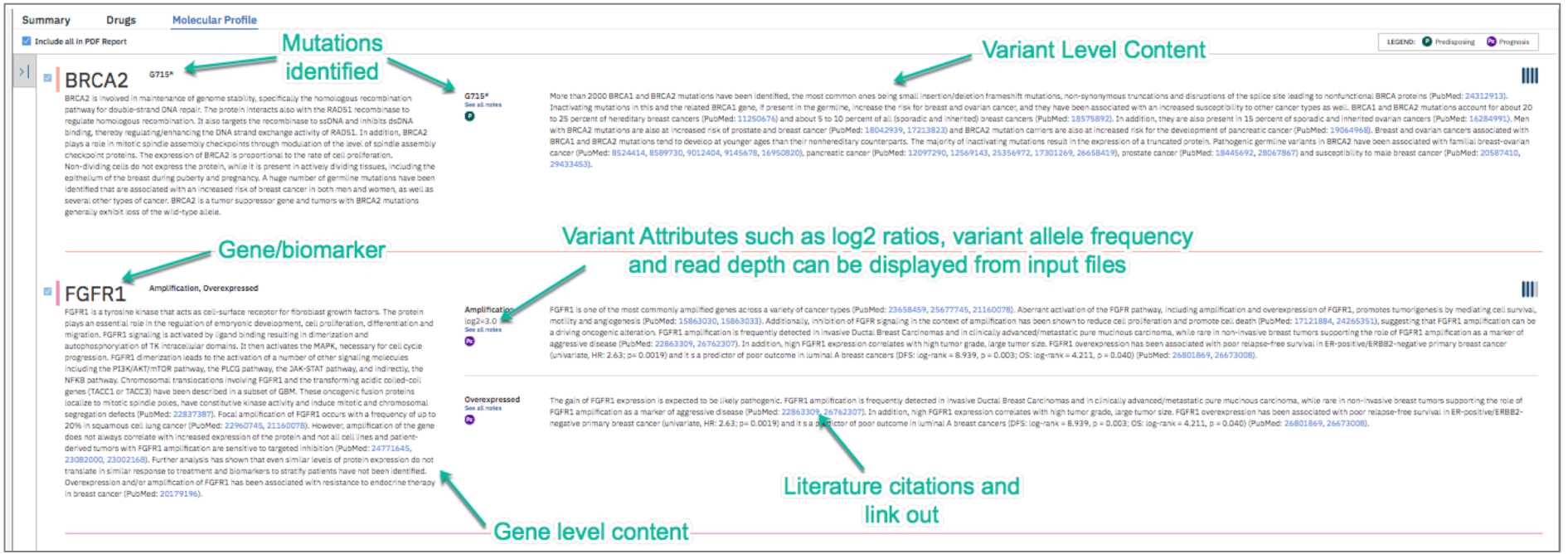
- Each targeted therapy or immunotherapy option match is associated with a level of evidence
- Incorporates drug responsiveness and drug resistance information
- Level of evidence factors into degree of cancer specific clinical relevance of a biomarker in Watson for Genomics

Evidence sources:

- FDA drug labels
- NCCN guidelines
- Case studies
- Clinical and preclinical evidence from the published literature
- Chemotherapy options **not** included

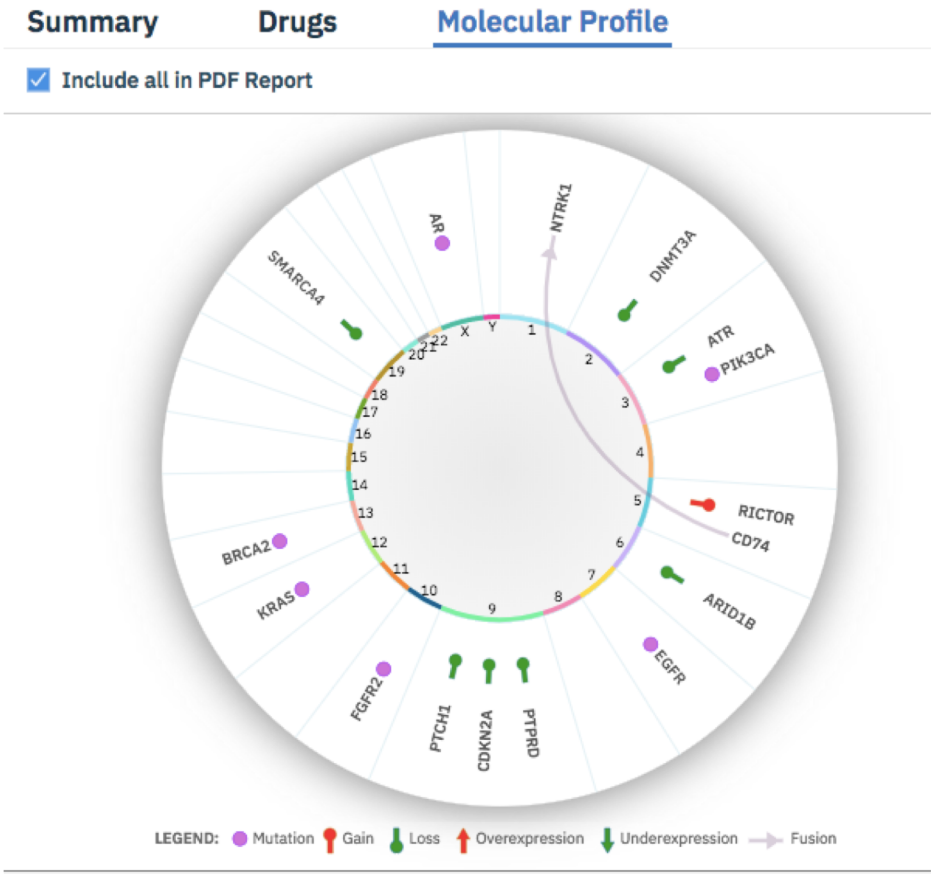


Mutation list format



Circular plot format

- Global view of all the mutations in the sample
- Organized by chromosome
- Indication of the functional impact of the mutation (e.g, overexpression)
- TMB (if high) also represented within the circular plot
- Interactive: clicking on a gene directs you to its detailed information in the table



Clinical Trial Association

Watson for Genomics matches the patient's molecular profile to available clinical trials with:

- Targeted therapies
- Immunotherapies

Patient information: age, gender (if provided), ER/PR/HER2 (if breast cancer)

Cancer type

Genetic profile

Drug list

Clinical trial details (sourced from clinicaltrials.gov)

Overview | Clinical Trials | Literature

TOTAL: 7 | Refresh Update: 2018-04-17

Targeted Agent and Profiling Utilization Registry (TAPUR) Study

NCT02693535

Conditions:	Status:	Interventions:
Solid Neoplasm	Phase 2 Recruiting	Pertuzumab, Sunitinib, Vismodegib, Erlotinib, Trastuzumab, Dasatinib, Axitinib, Olaparib, Cetuximab, Read More...

A Phase 2 Study of Olaparib Monotherapy in Metastatic Breast Cancer Patients With Germline or Somatic Mutations in DNA Repair Genes (Olaparib Expanded)

NCT03344965

Conditions:	Status:	Interventions:
Malignant Breast Neoplasm	Phase 2 Recruiting	Olaparib

Export and download of Watson for Genomics reports - Via User interface and via API

PDF download

- Direct PDF version of report can be downloaded.

JSON download

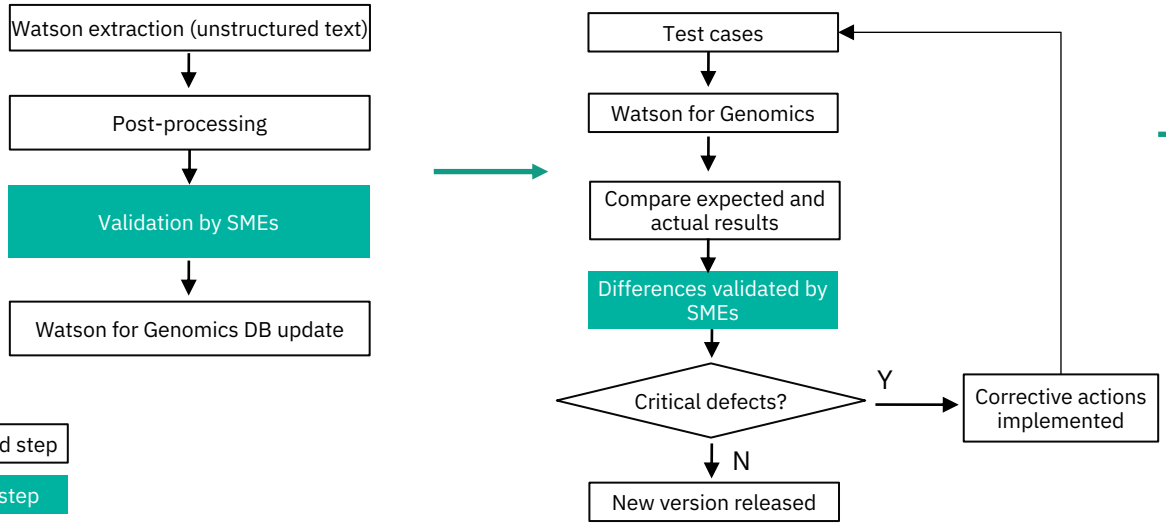
- Allows download of json reports that can be parsed for content customization or integration with client internal systems.
- Downloads an additional ‘filtered variants’ excel file to help clients analyze and troubleshoot if required.

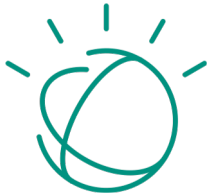
	A	B	C	D	E	F
1	Gene	Source	Annotation	Filtered Code	Filtered Reason	
2	CDK4	0.459431619		[P_E_007]	log2 value didn't pass the clinical thresholds (-2.000 -0.415 2.000).	
3	MET	-0.07400058		[P_E_007]	log2 value didn't pass the clinical thresholds (-2.000 -0.415 2.000).	
4	FGFR1	-0.40545145		[P_E_007]	log2 value didn't pass the clinical thresholds (-2.000 -0.415 2.000).	
5	MTOR	[1:11188229 G>null:NM_004958		[P_M_002]	Mutation is filtered out because variant type is not in scope.	
6	JAK1	[1:65312296 C>null:NM_002227		[P_M_002]	Mutation is filtered out because variant type is not in scope.	
7	MYCN	[2:16084127 G>null:NM_005378		[P_M_002]	Mutation is filtered out because variant type is not in scope.	
8	ALK	[2:29497924 C>null:NM_004304		[P_M_002]	Mutation is filtered out because variant type is not in scope.	
9	IDH1	[2:209113174 A111A>NM_005896		[P_M_002]	Mutation is filtered out because variant type is not in scope.	
10	PDGFRA	[4:55121532 G>null:NM_006206		[P_M_002]	Mutation is filtered out because variant type is not in scope.	
11	ALK	[2:29416366 G>C]		[F_M_008]	Mutation is benign. It is found 74.5% in EAS population from GNOMAD database.	
12	PDGFRA	[4:55133718 G>C:932-1G>A:NM_0062(		[F_M_004]	Inactivating (LOF) is in conflict with GOF role of PDGFRA in cancer.	
13	RET	[10:43617413 W917*:NM_020975		[F_M_004]	Inactivating (LOF) is in conflict with GOF role of RET in cancer.	
14	FGFR4	[5:176517797 C>T]		[F_M_008]	Mutation is benign. It is found 99.9% in EAS population from GNOMAD database.	
15	GNAQ	[9:80409379 C>C_G735A:NM_002072		[F_M_004]	Inactivating (LOF) is in conflict with GOF role of GNAQ in cancer.	
16	ALK	[2:29416572 T>C]		[F_M_008]	Mutation is benign. It is found 100.0% in EAS population from GNOMAD database.	
17	AKT1	[14:105246534>W22*:NM_001014431		[F_M_004]	Inactivating (LOF) is in conflict with GOF role of AKT1 in cancer.	
18	CDK6	loss-of-function		[F_G_003]	Functional Impact for the gene conflicts with GOF role of CDK6 in cancer.	
19	MYCN			[F_G_005]	None of the alterations in MYCN is in scope.	
20	CCND1			[F_G_005]	None of the alterations in CCND1 is in scope.	
21	TMB	TMB count: 11 muts, TMB normalizec		[F_T_002]	TMB didn't exceed the threshold.	

Artificial intelligence used to amplify the curation process

Literature Refresh

Expert Validation



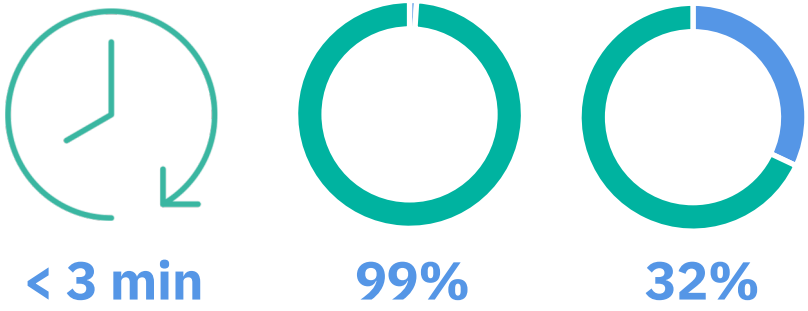


Watson for Genomics interpretation

The Oncologist 2017;22:1–7, Supplemental Materials

The Oncologist: Watson for Genomics found 99% of the actionable mutations identified by the molecular tumor board

Patel N, et al. The Oncologist. 2018;23(2):179-185.



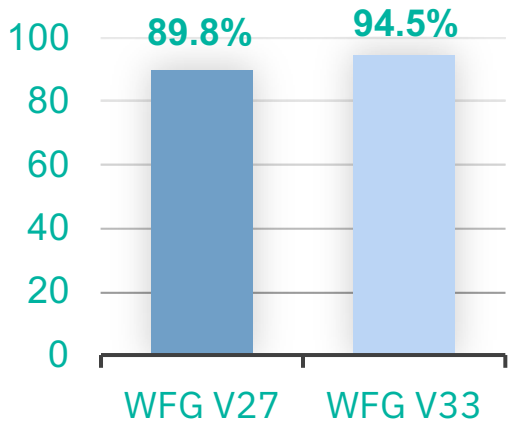
Watson for Genomics took less than 3 minutes per case. Found 99% of the actionable mutations identified by UNC's MTB and identified additional actionable mutations that the MTB did not in 32% of the cases (N = 1,018)

"Molecular tumor boards empowered by cognitive computing can significantly improve patient care by providing a fast, cost-effective, and comprehensive approach for data analysis in the delivery of precision medicine." -The Oncologist

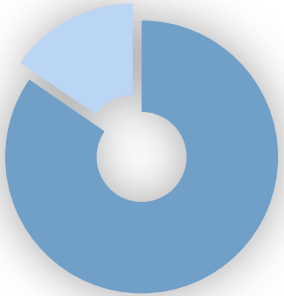
*excerpt from manuscript

Frontiers in Medicine: Evaluating clinical genome sequence analysis by Watson for Genomics

Itahashi, et al. Frontiers in Medicine. 5:305. doi:10.3389/fmed.2018.00305, 2018



Concordance between WfG and expert panel for mutation pathogenicity (N = 198); 12 months between versions



84.6%

Concordance between WfG and expert panel for targeted therapies (N = 198)

"WfG [Watson for Genomics] may be useful in cases where large amounts of genomic data is available, such as whole exon sequences, and in institutions with an insufficient number of experts in gene analyses."

*excerpt from manuscript

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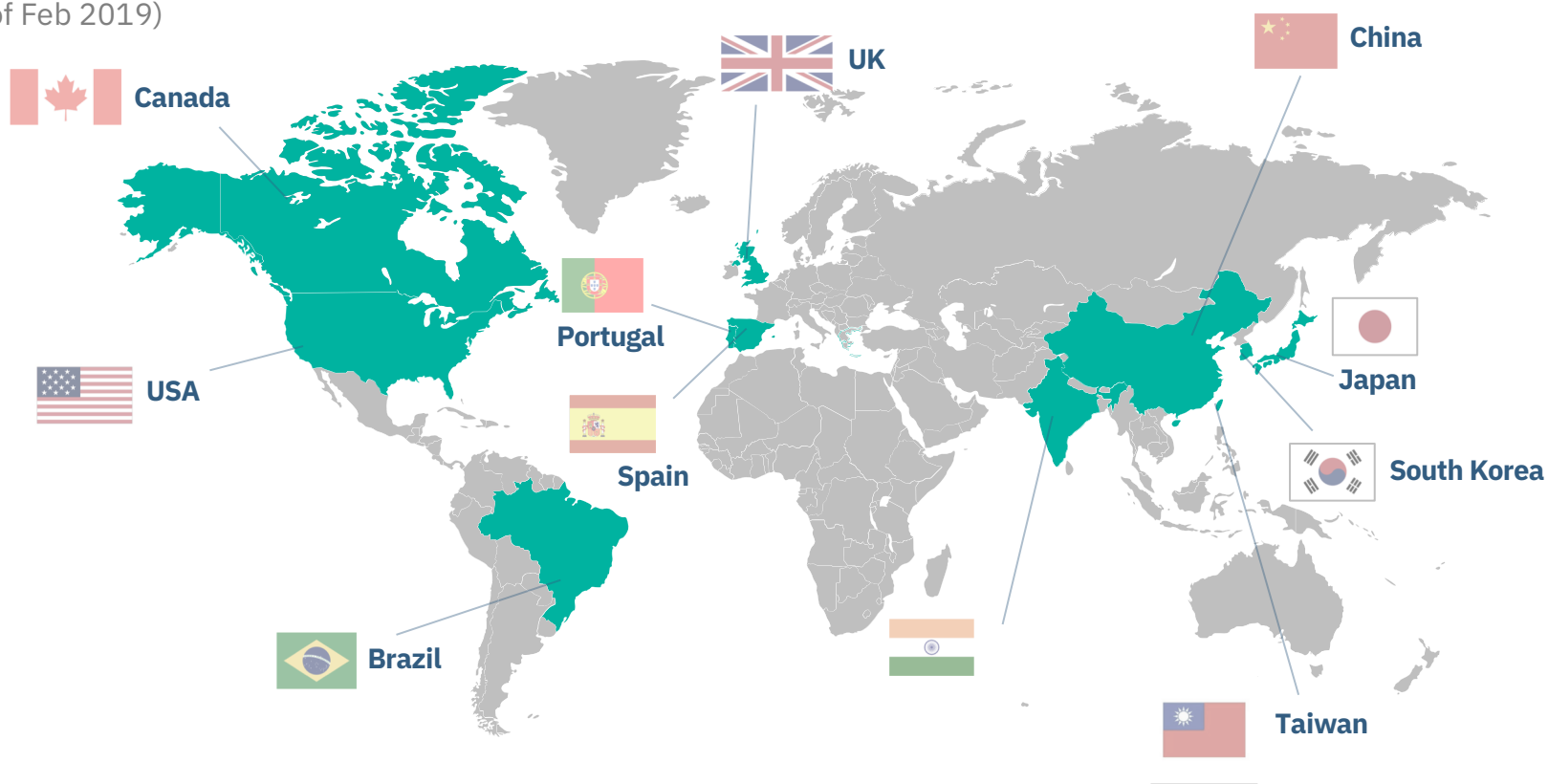
Appendix

Watson for Genomics : Worldwide implementations

(as of Feb 2019)



Our vision

Leverage AI to provide expertly validated, up-to-date, comprehensive content to enable clinical reporting

Value:

- Expertly curated, variant information and clinical content based on the latest therapeutic options, professional guidelines, clinical trial options and relevant publications.
- Clearly defined level-of-evidence model, including clinical and pre-clinical information.
- Rapid, efficient, and reproducible interpretation across cancer types
- Easily scale sample volume and complexity of gene panels — from targeted panels to whole genome.

Watson for Genomics ingests diverse inputs

Application	Information type	Supported format
Substitutions and short indels	SNVS and indels	.vcf or .maf *
Copy number change	Copy number variants	.log2 or .vcf
Gene rearrangements	Fusions/ translocations	.fusion or .vcf
mRNA differential expression	Gene expression data	.dge
Immuno-oncology biomarkers	Tumor Mutation Burden & Microsatellite Instability	TMB: .vcf or TMB value/status MSI: Status (High, Low, Stable)

- Uploaded files for each case can contain either a .vcf or .maf but not both
- Watson for Genomics supports GRCh37/ hg19