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Discover the benefits of automated clinical variant interpretation for your molecular tumor profiling

MH Guide interprets complex genetic data quickly and accurately to meet the growing challenges of sequence variant interpretation today and tomorrow

IVDR
(EU) 2017/746

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

Clinical Laboratory Improvement Amendments

MH GUIDE

This might interest you:

1

The benefits of MH Guide

Automated variant interpretation – fast, precise, efficient

MH Guide is an in-vitro diagnostic software approved in Europe under (EU) 2017/746 (IVDR) and certified and accredited under CLIA/CAP in the USA. It assists healthcare professionals in the examination of next generation sequencing (NGS) data or genetic and molecular alteration data to provide information to aid in the determination of treatment options based on genetic biomarkers and medical guidelines for patients diagnosed with cancer (solid and hematological tumors). Independent of the sequencing technology used, MH Guide can interpret complex datasets and automatically identify genetic variants that are relevant for the treatment of cancer patients to support you in identifying individual therapy options.

How laboratories benefit from MH Guide

- Automated interpretation of NGS data for small and large panels, as well as whole-exome sequencing (WES) and data from other compatible analytical methods
- Access to comprehensive, up-to-date variant interpretations through Dataome, one of the world's largest databases for biomedical information
- Rapid, quality-assured clinical variant annotation and report generation
- Highly customizable results report: users can filter for relevant information and integrate their own data and sources
- Digital platform for interdisciplinary case discussion in molecular tumor boards

The MH Guide process

Diagnostic and molecular pathology laboratories use our software-based in-vitro diagnostic application MH Guide to identify relevant biomarkers in tumor samples, and to provide attending physicians with information on individual treatment and trial options.

The software compares the patient sample data with current, published biomedical knowledge and drug information. MH Guide provides pertinent information about identified, relevant biomarkers and their clinical significance in the respective cancer entities. All of this information is summarized in a clear patient report. You can customize this report and integrate it in your pathology report, and for tumor board discussions.

This way, clinical colleagues quickly receive conclusive findings: all of the key information on effective and safe drug treatment options and available clinical trials – entirely in line with precision medicine.

Data Security with MH Guide

- Molecular Helath employs advanced encryption standards (SSL/TLS, AES-256) to safeguard patient data and stores it with controlled access authorization
- Molecular Health utilizes data centers certified according to international security standards, including Trusted Site Infrastructure (TSI) and ISO 27001:2013
- Molecular Health performs third-party penetration tests and maintains a continuous process for vulnerability scanning and handling

Data Privacy with MH Guide

MH Guide meets the requirements of:

- General Data Protection Regulation (GDPR) in Europe
- Health Insurance Portability and Accountability Act (HIPAA) in the USA
- Genetic Diagnostics Act (GenDG) in Germany

2 Big Data analytics for labs

Automated variant interpretation with data from Dataome – the “learning database”

The Dataome knowledge base is the foundation for the MH Guide analysis platform. Developed over a decade, Dataome is a proprietary global data platform for biomedical knowledge that combines three innovations:

Dataome Capture:
The platform uses artificial intelligence and machine learning to mine molecular and clinical data sources in real time. For clinical variant interpretation, data is curated by experts (molecular biologists, molecular pathologists, oncologists).

Dataome Knowledge:
Dataome screens and bundles the world’s medical literature. This allows analysis data to be placed in a medical context.

Dataome Analytics:
Complex genetic tumor data, such as NGS data, is efficiently and automatically matched by MH Guide with information obtained from Dataome and used for clinical variant interpretation.

3 Clinical variant interpretation

Precise translation of variant interpretations into treatment options

MH Guide combines the variants, pre-classified according to ACMG standards[1], with therapy-relevant findings – and lists the relevant information:

- Identified variant (germline or somatic, zygosity)
- Disease associated with the variant
- Validity of identified predictive, prognostic, and diagnostic biomarkers
- Display of gene impact (oncogenes, tumor suppressor, and HRR genes)
- Display of variant impact (e.g. activation, deactivation, switch of function)
- Impact and approval status of potential treatment options
- Suitable clinical trials, if available
- Summary of clinically relevant variant interpretations
- Pre-classified variant oncogenicity assessment based on ClinGen/CGC/VICC recommendations[2]

[1] Richards S et al.,Genet Med 2015
[2] Horak P et al., Genet Med 2022

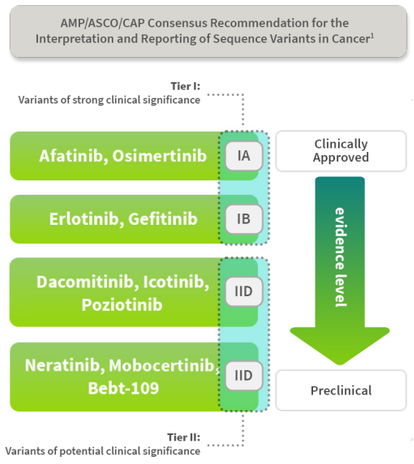
Flexibility and transparency of variant evaluation

- The MH Guide analysis can be customized by setting filters or implementing rules
- MH Guide gives the user full access to the evidence base of clinical variant interpretation

The Clinical Variant Interpretation (CVI) narrative with MH Guide*

EGFR p.S768I | **Lung Adenocarcinoma**

EGFR is a receptor tyrosine kinase that regulates the PI3K and RAS/MAPK pathways. In preclinical studies, the variant S768I activated both pathways. The S768I mutation accounts for about 0.49% of all EGFR mutations and often appears as a complex pattern with other EGFR mutations. Afatinib is indicated for the treatment of lung adenocarcinoma with EGFR mutations, including S768I. In the LUX-Lung 2/3/6 clinical trials, tumors carrying S768I as a single or combined EGFR mutation responded to afatinib treatment (objective response rate 100%). Osimertinib is indicated for NCSLC with activating EGFR mutations (EMA). This mutation is often reported to co-occur with additional mutations, such as L858R, G719X, or exon 19 deletions. In a few case reports, lung adenocarcinomas with this mutation were sensitive to the EGFR inhibitors gefitinib, icotinib, and erlotinib, though to a lesser extent than those with more common EGFR activating mutations, such as L858R. Tumor responses in patients treated with dacomitinib, osimertinib, and poziotinib were also described. Cell lines with this mutation are sensitive to dacomitinib, neratinib, BEBT-109, and mobocertinib but exhibit reduced sensitivity to gefitinib and erlotinib.



[1] Li, MM et al., J Mol Diagn 2017

*This is a representative example of an MH CVI narrative. Narrative content such as indications, biomarkers, variant-drug relations, drug approvals, and illustrations may change over time with MH Guide software and content updates.

The components of MH Guide Clinical Variant Interpretation (CVI)

Based on data derived from Dataome, MH's exclusive knowledge base, pertinent information for interpreting clinical variants is compiled within the context of each patient case and presented for MH Guide users in standardized CVI narratives, which can then be used in the MH Guide report. The exhaustive presentation of all information in the CVIs dramatically reduces and streamlines the time required for comprehensive interpretation of identified variants. The CVIs contain details on identified variants and their distinct descriptions, specifying the type of biomarker (predictive, diagnostic, prognostic), source citations, a clinical evaluation of biomarkers based on internationally recognized tiering systems (AMP/ASCO/CAP joint consensus recommendations), the treatment options' approval status, and more.

Region-specific Content

MH Guide offers region-specific content matching based on the patient's location, including:

- Information on drug approvals specific to e.g., the USA (U.S. Food and Drug Administration, FDA) or the European Union (European Medicines Agency, EMA)
- Details on region-specific clinical trials, including distance calculations to help minimize inconvenience to patients
- Recommendations and practice guidelines for cancer treatment from leading medical oncology networks and societies, e.g., NCCN (National Comprehensive Cancer Network) and ESMO (European Society for Medical Oncology)
- Regional clinical tiering systems will be available through MH Guide, such as the European ESCAT system and the German DKTK/NCT system

Evidence-based decision aid for treatment planning

The interactive MH Guide report gives an overview of all the important information on the biomarkers detected in a tumor sample. It includes the variant name as well as biomarker assessment and clinical validity according to international guidelines (AMP/ASCO/CAP JCR).

For treatment planning, the MH Guide report provides an overview of:

- Potential treatment options
- Potentially ineffective drugs and those with safety concerns
- Information on relevant, recruiting clinical trials

The report can be supplemented by integrating analysis results from non-NGS methods such as FISH, IHC, or qPCR, and can be individualized and integrated into the local infrastructure thanks to standard digital formats.

Report output formats are PDF, JSON, and XML

MH Guide features structured export of all variant information in CSV format for single and multi case analysis

Everything at a glance:

Electronic signature of the pathologist in charge

Patient, sample, and order information

Summary statement

Summary of detected biomarkers, therapy options, approval information, and clinical trials

- Effective
- Ineffective
- Possible safety risk

Regulatory agency information on approved biomarkers

Identified pathogenic variants

GUIDE

Patient ID Demo_NSCLC_TSO-001 **Diagnosis** Lung cancer
Case ID EU009700 **ICD-10 code** C34.31
Date of birth 09 Feb 1954

PATIENT

Patient ID	Demo_NSCLC_TSO-001
Case ID	EU009700
Date of birth	09 Feb 1954
Sex	Male
Country	DE

SAMPLE

Primary tumor site	Lung
Tissue type	Lung
Metastatic	yes
Tumor cellularity	90%
Collected	01 Feb 2023

ORDER & REPORT

Ordered by	Elisabeth Ryan
Facility	Sunnyville Hospital
Labtest	VCF Illumina TSO500 Panel (unpaired)
Order date	06 Feb 2023
Signed by	Marc Rauschendorf
Signed on	13 Oct 2023
Version	11

INTERPRETATION

Based on the patient's molecular profile and on evidence from publications, Osimertinib should be considered the preferred treatment option for the patient.

SUMMARY OF GENOMIC AND BIOMARKER FINDINGS

Detected biomarkers with therapy implications:

BIOMARKER	VAF (%)	APPROVED TREATMENTS FOR PATIENT DISEASE	BIOMARKER SCORE	TRIALS	OTHER TREATMENTS	DRUG APPROVAL	BIOMARKER SCORE	TRIALS
EGFR p.E746_A750del	29.52	E Osimertinib	I A 7 EMA FDA	4	E Aumolertinib	Investigational	I B 6	0
		E Afatinib	I A 7 EMA FDA	0	E Alflutinib	Other	I B 6	0
		E Dacomitinib	I A 7 EMA FDA	0	E Nazartinib	Other	II D 5	0
		E Erlotinib	I A 7 EMA FDA	0	E Mobocertinib	Investigational	II D 3	0
		E Erlotinib Ramucirumab	I A 7 EMA FDA	0	E Zipalertinib	Investigational	II D 3	0
		E Gefitinib	I A 7 EMA FDA	0				
Additional biomarkers#		Diagnostic: TP53 p.P152L (n/a, 6)						

E Effective: potentially effective treatments

Biomarker score: AMP/ASCO/CAP category and CVI score. See the glossary for more information.

See Biomarker details section for more information.

PATHOGENIC VARIANTS

Identified pathogenic and likely pathogenic variants:

VARIANT	CODING DNA	TYPE AND EFFECT	VAF (%)	CLASSIFICATION
TP53 p.P152L	ENST00000269305.4 c.455C>T	SNV Missense	32.98	Pathogenic
EGFR p.E746_A750del	ENST00000275493.2 c.2235_2249del	del In-frame	29.52	Likely pathogenic

MOLECULAR HEALTH
Molecular Health GmbH
Kurfuersten-Anlage 21
69115 Heidelberg, Germany
+49 6221 43851-150
CustomerService@molecularhealth.com

MOLECULAR HEALTH

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How to reach Molecular Health

Molecular Health GmbH
Kurfuersten-Anlage 21
69115 Heidelberg
Germany, Europe

Tel.
(GER): +49 6221 43851-150
(US): +1 978 491 8393
CustomerService@molecularhealth.com

We develop and offer innovative technologies in the fields of in silico medicine and precision medicine

Our solutions enable the conversion of large amounts of data into evidence-based, medically relevant results for the actors in the healthcare sector. Therewith, we provide molecular pathologists, geneticists, physicians, and patients with better information on diagnoses and therapy options. We support pharmaceutical and health organizations by optimizing clinical studies in the development of promising active ingredients and meaningful disease models.

Request a demo

Learn more about our certifications

MH-23-019-1EN