BiomeDx

Intended use of BiomeOne®

Overview of device
Name: BiomeOne
REF number: B1
Regulation: Directive 98/79/EC of the European Parliament and of the Council
Classification: Other IVDD

Name and address of the manufacturer
Biome Diagnostics GmbH
Handelskai 92/Rivergate/Gate 2/1.OG/B+G
AT - 1200 Vienna
AUSTRIA

Intended purpose

BiomeOne® is a cloud-based in vitro diagnostic software intended for the detection of responders and non-responders to checkpoint inhibitor based cancer immunotherapy (CTLA-4, PD-1, PD-L1) based on stool microbiome profiles of late-stage cancer patients. The product encompasses the proprietary microbiome profiler for response prediction and the platform service provided to healthcare professionals to order the kit and analysis, and download the analysis report. The cloud-based nature of the software is able to store, transfer and analyse FASTQ files from next-generation-sequencing platforms and generate a PDF report containing the predicted response information. The diagnostic software performs bioinformatic workflows and infers response to checkpoint inhibitor based cancer immunotherapy using a proprietary microbiome profiler based on statistical algorithms of microbiome samples from patients with non-small cell lung cancer, renal cell carcinoma and malignant melanoma.

The results described in the BiomeOne report are intended as additional information for the treating physician and should not be used as the sole basis for any treatment decision. BiomeOne should only be used by qualified healthcare professionals. It provides clinically relevant and reproducible, quantitative data for improving therapy management.

The primary performance study was conducted in the following three tumour types: non-small cell lung cancer, renal cell carcinoma, and malignant melanoma. Female and male participants were included in the study to equal parts. BiomeOne is indicated for in-vitro diagnostic use with a response prediction sensitivity of > 80%.

As a result, the clinical oncologist who ordered the BiomeOne analysis receives a PDF report with information regarding the predictive signature of response and irAEs and analytical information regarding the health of the patient's intestinal microbiome. BiomeOne does not inform the decision, but rather supports it, and should be used together with other adequate diagnostic tests, evaluation of clinical history of each individual patient and other relevant

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AT – 1200 Vienna
Tel.: +43 660 357 28 93
Email: office@biome-dx.com
Web: www.biome-dx.com
HR-Nr.: FN501216h
VAT.-ID: ATU73865506
Tax-No.: 22 331/4980

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Description of BiomeOne®

BiomeOne® is a cloud-based medical diagnostic software consisting of multiple subcomponents that store, transfer and analyse FASTQ genetic files from common microbiome sequencing platforms (e.g., Illumina) and anonymised medical data. The diagnostic software takes as input data FASTQ files from Illumina's BaseSpace or other connections (e.g. SFTP, API), applies bioinformatic workflows and implements a proprietary microbiome (immune) profiler based on statistical algorithms derived from metagenome sequencing information of stool samples from patients with non-small cell lung cancer, renal cell carcinoma and malignant melanoma who are eligible for immune checkpoint inhibitor therapy. The software is designed to run as a cloud service (SaaS) accessible for professional use through common web browsers (e.g., Google Chrome) via the BiomeDx Platform and displays the results in a printable PDF report. The results of the companion diagnostic software assist clinical oncologists and qualified healthcare professionals by computing a probability of tumour response to checkpoint inhibitor therapy and possible immune-related adverse events (irAE). It provides reproducible, clinically-relevant quantitative data for improving therapy management based on the predicted outcome, and has been tested and validated on 16S sequencing data acquired using Illumina sequencing.

Stool samples are collected by the patient using at-home collection stool tubes with a preservation fluid manufactured by Norgen Biotek (or similar). Due to the high microbial density of stool, sterility is not a requirement when collecting the sample. The proposed laboratory analysis for BiomeOne performs DNA extraction from the faecal microbiome sample, with about 50 - 1000 ng of which undergo 16S library construction and amplicon sequencing of the hypervariable region V3-4, resulting in amplicons with an average size of 460 base pairs. Using the Illumina platform, the libraries are sequenced to a highly uniform depth targeting 50.000 paired-end reads. BiomeOne uses bioinformatic workflows to process the resulting FASTQ files of each patient´s microbiome sample and correctly identifies bacteria species in the stool sample. Subsequently, the species information is matched with the proprietary microbiome profiler of Biome Diagnostics to classify therapy response and adverse events to immunotherapy. A BiomeOne report is generated and provided for professional use to clinical oncologists.

BiomeOne software is intended to be used as a support tool by trained healthcare professionals in accordance with professional guidelines in oncology to aid in therapy evaluation. It is intended to provide microbiome and related information that is interpreted by a trained professional to evaluate suitability for immune checkpoint inhibitor treatment before therapy initiation, but it does not directly generate any diagnosis or treatment recommendation. The software is contraindicated for analysing microbiome data that are acquired on sequencers from manufacturers other than Illumina or its subsidiaries or from patients not conforming the intended patient group.

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CE-marked software components

- bix-project-service: Retrieve and store FASTQ files
- bix-16s: BiomeOne bioinformatic workflow
- ml-biomeone: BiomeOne microbiome signature
- report-service: Generate PDF report
- biomedx-platform: Platform to handle all involved logistic (order
    - analysis, download report)

Results included in the report

- Predictive signature
    - Probability of response (CE-IVD)
    - Probability of immune related adverse events (RUO)
- Analytical signature
    - Enterotype
    - Shannon diversity o Bacterial richness
- Density plots for response and irAEs
- Bacteria list and values found in the sample

Indication(s)

- To be used in cancer patients with stage III/IV of one of the following cancer tumour types: non-small cell lung cancer, renal cell carcinoma and melanoma.

Intended user group

- Clinical oncologists and qualified healthcare professionals are able to order stool kits related to BiomeOne analysis online via the BiomeDx Platform.

Intended patient group

- Stage III/IV cancer patients with one of the following indications
    - Non-small cell lung cancer
    - Renal cell carcinoma
    - Melanoma
- Male & female aged 18 to 90 years

Contraindications

- Systemic antibiotic treatment may influence the analysis results due to their detrimental effects on the intestinal microbiome. It is advised to wait at least 30 days after the last administration of systemic antibiotics before a stool sample is taken.

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Legal clarification

The information in the report must be considered in conjunction with all other relevant information regarding a particular patient, before the patient's treating medical doctor recommends a course of treatment.

UMDNS/GMDN classification

66126 - Human microbiome analysis interpretive software IVD

Performance attributes

BiomeOne can predict the response of cancer patients with the following probability metrics, as validated in a clinical study:

Metrics	Probability
Sensitivity	81%
Specificity	52%
Positive predictive value	77%
Negative predictive value	58%

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