# BiomeOne®: multi-centric validation of a novel microbiome-based test to predict response to cancer immunotherapy

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## INTRODUCTION

- The intestinal microbiome has a substantial influence on the cancer-related response to immune checkpoint inhibitor (ICI) therapy.
- Biome Diagnostics (BiomeDx) has developed **BiomeOne®**, a tumor-agnostic **CE-IVD marked medical device** that uses baseline **stool samples** to analyse the intestinal microbiome and predict patient **response to ICI**. The biomarker was developed using datasets from stool samples of previously studied patients with non-small-lung-cancer (NSCLC), renal cell cancer (RCC), melanoma, and a healthy cohort ($n$=8,000).
- **The aim of our study was to evaluate the prognostic potential of BiomeOne® in a cohort of NSCLC, melanoma and RCC patients.**

## METHODS

- **Stool samples** collected with at-home kit (Norgen Biotek), **prior to ICI treatment** initiation and at **week 12**;
- **16S rRNA sequencing** was performed with Illumina MiSeq® at a central laboratory;
- 1400 species were identified which were then transformed into a robust low-dimensional representation using an autoencoder. **Machine learning** (ML) algorithms were applied to determine a specific microbial signature, named BiomeOne®.
- **Clinical response** was assessed at the end of first line therapy. **Responders (R)** were classified as complete and partial responders (CR, PR) and **non-responders (NR)** as stable and progressive disease (SD, PD). Best response was compared with the outcome of BiomeOne® analysis.

## RESULTS

- **65 patients**: NSCLC (42), RCC (16) and melanoma (7) were enrolled. Patients were treated with ICIs targeting CTLA-4, PD-1 or PD-L1 as well as combinations with TKIs. No systemic antibiotic treatment 30 days prior to ICI therapy initiation;
- Overall, **63 including 42 responders and 21 non-responders completed first line treatment**. BiomeOne® was able to identify responders to ICI treatment with a **sensitivity of 81%** and a **positive predictive value of 77%;**
- ML analysis did not depict significant differences between the 3 tumour types, suggesting that the biomarker is tumour agnostic.

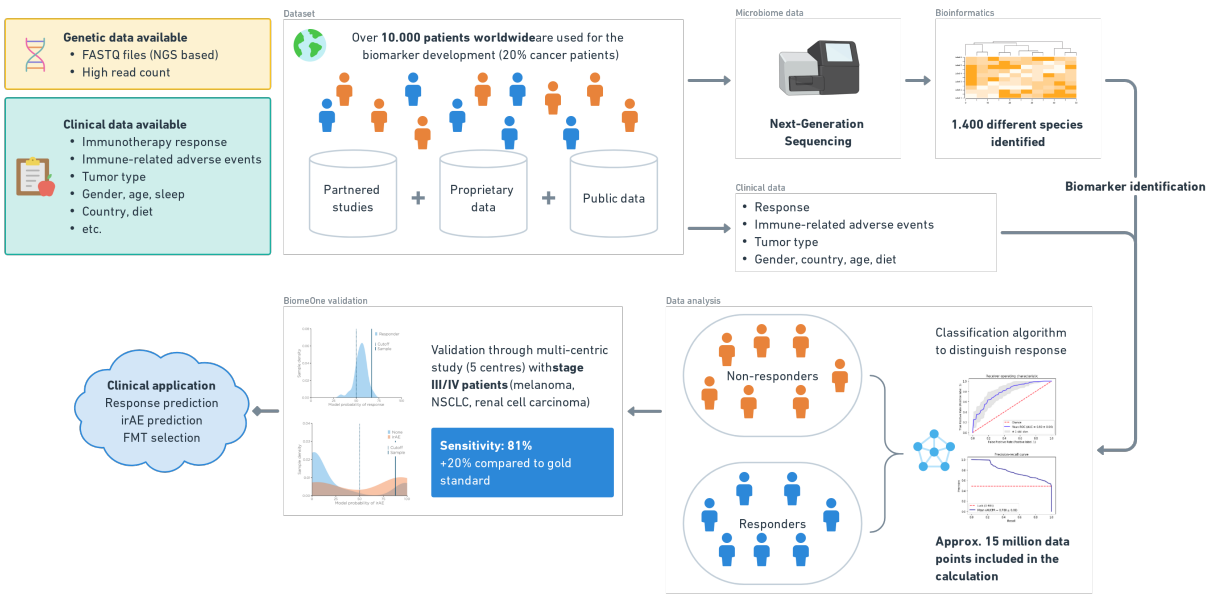


Figure 1. Schematic representation of model development for microbiome profiling of response to ICIs (=training dataset).

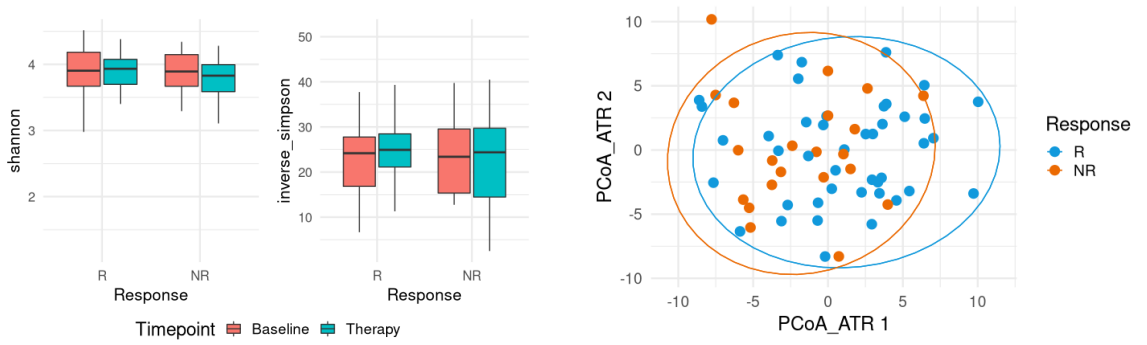


Figure 3. **Alpha-diversity** indices Shannon (P = 0.30) and inverse Simpson (P = 0.37) **did not differ between R and NR nor between baseline and week 12** (P > 0.77). **Beta-diversity** did not differ between R and NR (P > 0.05).

- *Suterella* sp., *Faecalibacterium* sp. and *Haemophilus* sp. were found to be differentially abundant between R and NR (P < 0.05).
- No significant differences between the 3 tumour types, suggesting that the **biomarker is tumour agnostic**.

Table 1. Comparison between BiomeOne® results and clinical response.

| | **Responder** CR + PR | **Non-responder** SD + PD | Total |
|---|---|---|---|
| **BiomeOne: High** | 34 (pass) | 10 (fail) | **44** |
| **BiomeOne: Low** | 8 (fail) | 11 (pass) | **19** |
| Total | **42** | **21** | **63** |

- BiomeOne® was able to identify responders to ICI treatment with a **sensitivity of 81%** and a **positive predictive value of 77%.**

## CONCLUSION

The presented research demonstrates the potential of BiomeOne® as a novel, non-invasive test to predict the outcome of ICI therapy. Further research will be necessary to expand the scope of BiomeOne® to other tumour entities.

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