

IVAC® - Individualized Vaccines Against Cancer Platform

The Platform

Every tumor has an exclusive pattern of shared tumor antigens and mutations, which makes every tumor absolutely unique. At BioNTech, we use these tumor-specific antigen signatures to generate treatments for each individual patient. We have developed the Individualized Vaccines Against Cancer (IVAC®) platform using tumor-specific information combined with our RNA-platform technologies to tailor each patient's personalized immunotherapy. The goal is to activate the immune system of

each patient to recognize, target and fight the individual cancer. To effectively reach this goal, we have developed two IVAC® concepts – IVAC® WAREHOUSE and IVAC® MUTANOME. Both concepts allow us to design custom-made IVAC® vaccines for every single patient individually (Figure 1 and Figure 2). We are pioneers in moving this RNA-based concept of truly personalized therapy into the clinic.

The IVAC® platform is characterized by:

- Fast, cost-effective and flexible production
- Favorable safety characteristics of synthetic RNAs
- High grade of flexibility allowing fast integration of technical improvements
- Versatile use of the two IVAC® concepts as individual or combination strategies

IVAC® WAREHOUSE Process

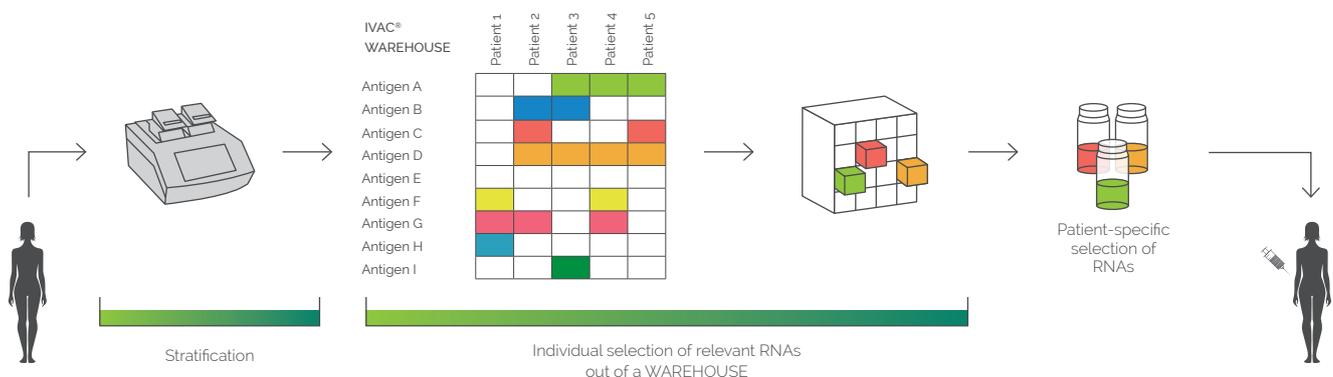


Figure 1: Patient's tumor will be profiled by RT-qPCR for the specific antigen expression profile. The resulting data will be actively used to select a personalized set of RNAs for a given patient. This process from delivery of the sample to the output of the test results has a typical turnaround time of two days allowing a fast treatment decision. Each patient will thus receive an individual combination of RNAs from the warehouse that corresponds to the patient's antigen-expression profile.

IVAC[®] MUTANOME Process

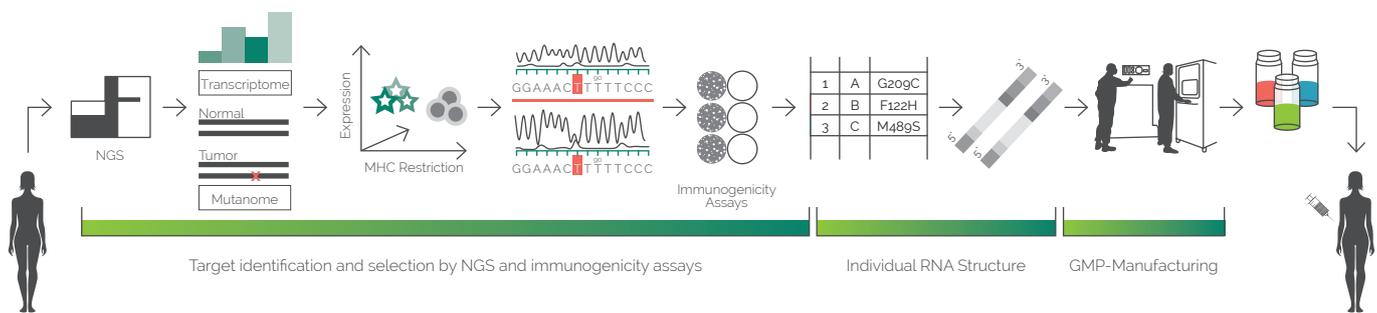


Figure 2: Somatic mutations in a patient's tumor are determined by NGS, prioritized and confirmed following a well-defined process. Furthermore, the patient-individual immune status is investigated by an immunogenicity assay. The mutations are then ranked and selected according to their relevance followed by the lead structure design. Finally, the GMP-grade synthetic messenger RNA vaccine that encodes patient-specific sequence stretches incorporating non-synonymous mutations is manufactured.

The Science

We are using our proprietary IVAC[®] platform to develop personalized immunotherapies for potentially all cancer indications.

The IVAC[®] WAREHOUSE concept is based on the development of RNA-based vaccines that target shared tumor-associated antigens. The antigens that are included in a warehouse are carefully selected based on their selective expression in a certain tumor entity and their ability to induce antigen-specific immune responses. Tumor material of a patient is profiled by RT-qPCR and based on the results, the most suitable RNAs are selected from the pre-manufactured IVAC[®] WAREHOUSE. The patient is then treated with an individualized vaccine that best matches the antigen profile.

The IVAC[®] MUTANOME concept aims at targeting unique tumor antigens that result from tumor-specific mutations. The IVAC[®] MUTANOME vaccine is produced de novo based on a patient's mutation profile. The IVAC[®] MUTANOME process starts with sequencing the patient's healthy and cancerous tissue using state-of-the-art next-generation sequencing (NGS) technologies. A proprietary algorithm compares the sequences in healthy and cancerous tissue and produces a catalogue of all tumor mutations, the tumor mutanome, which is specific for each patient. For the most suitable mutations, our cutting-edge platform technology for fast design, manufacture and release of truly personalized RNA-based IVAC[®] MUTANOME vaccines will be used.

In order to increase the availability of IVAC[®] MUTANOME vaccines for a larger cohort of patients, future enhancements of the technology are focusing on process optimization and automation. Economy-of-scale-effects and just-in-time production will make IVAC[®] vaccines available for large groups of patients.

Our Vision

... is to use IVAC[®] vaccines to make multiple cancers treatable and improve the survival of patients suffering from the most aggressive tumors.

... is to make the IVAC[®] platform a standard tool for personalized RNA-based cancer therapy.

Our Evidence

The IVAC[®] technology is a milestone for the development of personalized cancer vaccines. BioNTech is currently testing immunotherapies that are based on the IVAC[®] WAREHOUSE concept, the IVAC[®] MUTANOME concept or a combination thereof in several human clinical studies. By now, more than 40 pati-

ents have received at least one of our RNA-based vaccines. We observe a very favorable safety profile. We are convinced that further benefits of our personalized RNA-based immunotherapies will unfold in the ongoing and in upcoming clinical studies.

IVAC[®] is a registered trademark of BioNTech RNA Pharmaceuticals GmbH in Germany and other countries.