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Instand-NGS4P Phase 1

Short Publishable Summaries

Contents

Introduction

At the end of Phase 1, each Contractor was requested to provide a short publishable summary containing non-confidential information suitable for publication and for reading by patients´ organisations. These summaries are provided below.

LOT 1

Contractor: Agilent (Tender lead: Agilent Technologies R&D Marketing GmbH & Co KG)

We developed a complete workflow based on high-throughput sequencing that allows detection and characterization of all classes of genomic aberrations of cancer cells. A combination of selected tumour genes and genome wide features will allow informed decisions on treatment and/or prognosis. Additional features were included to increase data quality and predict a drug's efficacy, guide dosage and improve patient safety, respectively.

Contractor: IDT (Tender lead: Integrated DNA Technologies, BV)

IDT are proposing a comprehensive NGS workflow that advances existing technology and addresses current patient and clinical needs. It covers all steps of Lot 1 prior to sequencing and include 2 workflows including 1); Pre & Post PCR and 2); an automated “All-in-One” workflow configuration. This will provide the flexibility to accommodate various Medical Testing Laboratory requirements and laboratory operating procedures (ie. Linear flow SOPs) from low to high throughput laboratories. The workflow includes flexible solutions for nucleic acid (NA) extraction from various input sample types including FFPE, whole blood, plasma, serum, and urine. QC of NA involving quantification and normalisation and innovative NGS library preparation allowing efficient processing of low input and damaged patient samples into functional NGS libraries containing unique molecular identifiers (UMI) and unique dual indices (UDI). Library enrichment will utilise targeted, high quality Hybridisation Capture panels to detect novel and known variants, followed by QC of NGS libraries. The target panel design includes a Comprehensive Cancer Panel (CCP) of 379 genes, in addition to 17 targeted cancer specific sub panels that include targets from the CCP. The whole workflow is tightly controlled by usage of reference material targeting each gene of the CCP and an innovative solution for connectivity, sample tracking and information transfer. Our approach goes beyond current state of the art, by being automated, scalable, cost-effective, with improved performance and consideration of regulatory requirements. Altogether, our approach aims to improve cancer patient’s needs by implementing standardized and secure methods into routine diagnostics.

Contractor: Trinity (Tender lead: QIAGEN GmbH)

All diagnostic workflow stages including pre-analytical, analytical and post-analytical steps can influence final diagnostic analytical test results. During the development of NGS tests, all workflow steps therefore need to be specified, verified and validated. This includes especially pre-analytical workflows, which account in general for 50 – 70% of medical laboratory errors, mainly caused by post collection specimen changes. During Phase 1, we therefore prepared the development ofseveral new innovative NGS suited generic pre-analytical workflows. Preanalytical steps will include specimen collection, specimen preservation including analyte profiles stabilization, specimen storage, transport, processing and isolation of nucleic acids. It is of key importance that patient specimen analyte profiles are maintained during these steps as they were in the patient body.

Furthermore, future NGS tests sensitivity needs will not be achievable without such innovative pre-analytical workflows. Specimen typesin this project will include blood, bone marrow, tissues and different body fluids. Specimen target analytes will include cellular RNA, genomic DNA, different liquid biopsies nucleic acids as well as different cellular features. Multimodality and multisource specimen requirements will be taken into account, being especially important for cancer diagnostics. We will also develop optimized steps for linking pre-analytical workflows to NGS library preparation, including library quality control (QC). Current ISO & CEN Standards and EU IVDR 2017/746 requirements will be followed. Complete NGS workflows will be built with existing and upcoming new sequencing and bioinformatics solutions for judging the quality of the new pre-analytical / library solutions.

Contractor: TwistPlatomicsMGI (Tender lead: Twist Bioscience Corporation)

"**Standardized flexibility**" - even if it sounds contradictory, it´s exactly what is offered by the consortium of Twist Bioscience, Platomics GmbH and Latvia MGI Tech SIA (TPM) within the EU Horizon2020 tender "InstandNGS4P". The offered solution will allow oncologists and diagnostic labs to establish an individually tailored LDT solution, derived from the IVDR-compliant Master Panel. The physical sub-panels, including IVDR-compliant documentation will achieve this with significantly reduced effort (in setting up, documenting, validating etc.) and simultaneously offer so far unknown flexibility following a standardized procedure to ensure highest diagnostic quality.

Each of the three companies will add its strength to the common solution: MGI adds its expertise in nucleic acid extraction and nucleic acid- and NGS library quality control, for manual workflows as well as automated ones. Twist Bioscience adds its well-known, best-in-class NGS library prep and target enrichment solutions and design thereof. Platomics contributes its superior service in terms of bioinformatics and IVDR-compliant documentation service. Combining those strengths, the consortium will fulfil the needs of medical doctors, oncologists, human geneticists and last but not least the patients.

Today, labs have to use either restricted solutions in terms of analysable targets or have to apply large comprehensive, and very expensive panels. The TPM consortium's solution will allow the design and production of a tailored genetic diagnostics solution that meets both the individual labs general and more specific requirements. It will allow labs to conform to the highest standard of care and retain this standard through time.

LOT 3

Contractor: Cancer Analysis (Tender lead: Fundacio Centre De Regulacio Genomica)

The Cancer Analysis GPAP will enable streamlined and user-friendly management and analysis of NGS data in adult and paediatric cancers, common and rare. The platform will be based on the current RD-Connect GenomePhenome Analysis Platform [1], developed upon a big data architecture and a user-friendly graphical user interface (GUI), accessible through a web browser. The platform will have a modular design built upon Singularity containers, enabling installation in High Performance Computing (HPC) clusters and typical Cloud Computing Services. The modular approach will provide flexibility while facilitating updates and backups. Security will be incorporated in all the stages of the Software Development Life Cycle to take into account the EU GDPR and relevant ISO and IVDR requirements. All users will have to be authenticated in the system, which will use the OpenID protocol. The Cancer Analysis GPAP is structured around a well-defined and

streamlined workflow, envisioning different types of users, each with specific roles and permissions. A set of pre-defined, but still customisable, pipelines encoded with Nextflow and deployed with Singularity containers, will make it possible to analyse sequencing data input automatically according to the clinical request and the experimental information. Quality control metrics and messages will be provided at different stages of the process, providing flexibility to re-configure and re-launch steps through the GUI. The output will be VCF/gVCF files including annotated germline variants and/or somatic mutations, and BAM/CRAM alignment files. An automated verification solution with reference datasets will be implemented to ensure the desired accuracy is met.

Contractor: Congenica L3 (Tender lead: Congenica Ltd)

Congenica's system accurately recommends the right treatment for individual cancer patients (See Fig 1 below) and if appropriate, identifies Clinical Trials that a patient may be eligible for. It works by assessing adults and children's tumour samples to identify the genetic makeup of a patient's tumour and identifies the best treatment(s) for that particular tumour using the latest information from expert sources worldwide. It then analyses each patient's genetic makeup to understand how they process cancer medicines and provides recommendations based on this combined information. A clinical report will be sent directly to the clinician through the appropriate patient record system to be used when deciding a patient's course of treatment.

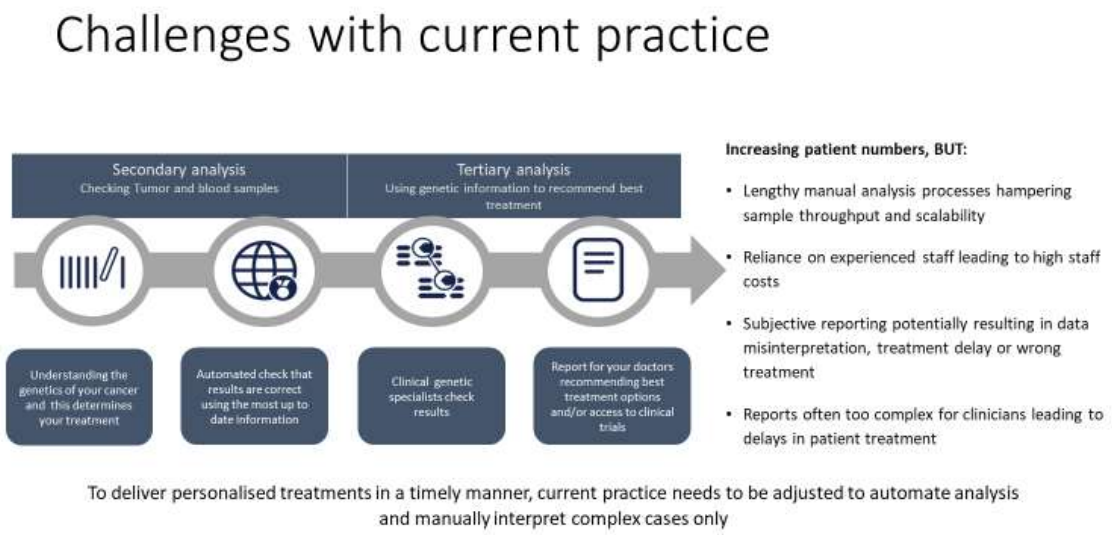

Figure 1

The Platform is designed to improve patient outcomes. Targeted treatment increases survival chances and can reduce side effects from medicines. Once a tumour is analysed a report can be with doctors in less than 7 days so they can quickly start accurate treatment (with minimal side effects), using medicine specifically recommended for each patient. The platform will meet the user and patient needs as identified in the tender specification and further enhanced through Congenica's own research. This procurement receives funding under the European Union's Horizon 2020 research and innovation programme under the grant agreement No 874719. The EU is however not participating as a contracting authority in this procurement 2 Patients will be given, via an App, their own secure version of the report with clear explanations of understanding of their condition, treatment and any recommendations for family and carers. The App will, if patients choose, share any genetic risks that might affect families.

Contractor: EU Onco-Platform (Tender lead: BC Platforms AG)

Our consortium is composed of three companies: BC Platforms (BCP), Euformatics (EUF) (both with R&D operations in Finland) and Oncompass Medicine (OCM) with R&D operation in Hungary. We plan to develop and add newly developed software modules in NGS4P to our existing, modular product portfolios from the three companies together and be able to go to market globally to address this universal need to generate clinical insights from genomic raw data in order to facilitate Precision and/or Personalised Medicine programs. This “EU ONCO-PLATFORM”, to be developed, will automate the processing of genomic data, provide best practice methods for finding genomic markers in patient sample’s genomic data and verify quality of the data in such a way that reliable insights from patient’s data can be obtained that help in finding the best treatment options for the patient. Our capabilities to automate, version and repeat NGS workflows ensure clinical repeatability. Our bioinformatics research and development, will ensure satisfaction for the Medical needs, by providing actionable variants for subsequent lots for final interpretation. All vendors in EU ONCO-PLATFORM have a long background in software development and customer implementations, and therefore can provide user friendly software solutions with appropriate expertise in documentation and training activities. All vendors in our consortium have already long experience in generating medical reports in NGS space, thus this experience will be most valuable in collaboration with Lot 4 winners, to satisfy needs for standardisation for medical reporting whilst keeping patient perspective clear throughout the process of development.

Contractor: INSPECT (Tender lead: Phenosystems SA)

To improve the cancer patients’ benefits from the Next Generation Sequencing (NGS) technology, our INSPECT consortium partnered with the Instand-NGS4P PCP project Buyers group to build a state of the art solution we call GensearchMax. GensearchMax is an NGS secondary analysis software solution that delivers accelerated and accurate genome analysis results to bioinformaticians, genome lab technicians, hospital genomics labs, and private labs. Unlike popular OS or commercial solutions, GensearchMax delivers integrated tools and (user-configurable) end-to-end automated workflows (from fastQ to VCF) to generate quick and accurate NGS results with pharmacogenomics in a secure and intuitive environment. GensearchMax will offer an unprecedented user experience for the analysis of NGS data from patients, offering the smart tools to define a pipeline adapted to patients' needs, validate it according to the latest IVDR requirements and use it, generating actionable knowledge for the treatment of patients in the secure environment. INSPECT consortium is made out of three partners who joined forces and expertise to deliver GensearchMax: Phenosystems, Maxeler/Groq and icoSys/HES-SO. Phenosystems has been developing user-friendly software solutions for the genetics and genomics laboratory since 2002 and collaborating with the icoSys group of the HES-SO since 2009. The icoSys group is specialised in distributed and high-performance computing and has contributed greatly to GensearchNGS, the current software commercialised by Phenosystems to clinical and research laboratories. Maxeler, which recently merged with Groq has extensive experience with HPC, AI and innovation and is on a mission to amplify GensearchMax performance and drastically reduce turnaround time to genome analysis results.

Contractor: PlatoDKFZCharité (Tender lead: Platomics GmbH)

PlatoDKFZCharité Consortium proposes OncOmicsX, an integrated NGS data analysis solution for IVDR-compliant NGS diagnostics parallelized with agile, highly tunable NGS data analysis for cancer patients. NGS-based diagnostics needs to be fully compliant with all applicable regulations. However, experience with thousands of patients discussed in molecular tumor boards (MTBs) has shown that it is impossible to meet all diagnostic needs and exploit the full potential of NGS-based diagnostics without evaluation of new and experimental biomarkers. OncOmicsX thus covers both in one comprehensive NGS data analysis platform: on one hand the ISO13485- compliant infrastructure PlatoX Somatic and on the other hand the flexible platform “One Touch Pipeline” (OTP). A core set of functionally equivalent workflows for alignment as well as germline and somatic variant calling are available in both parts. On the PlatoX side these workflows will be suitable for fully IVDR-compliant routine clinical NGS diagnostics, while on the OTP side they will allow the NGS analysis to go beyond strictly regulated IVDR “borders” to address additional translational questions in MTBs and to produce extended NGS data streamlined for research projects. The NGS analysis solution will also be integrated with a regulatory module, performing automated generation of regulatory documents for in-house manufactured devices (Laboratory Developed Tests) as demanded by the IVDR. The regulatory module will allow customers to accelerate and simplify the setup, validation, and documentation procedures for their own NGS tests and thus decrease the time required for innovations to transit from research into clinical adoption to provide patients with cutting-edge diagnostics.

LOT 4

Contractor: Cancer Reporting (Tender lead: Fundacio Centre De Regulacio Genomica)

The Cancer Reporting GPAP will be a user-friendly solution integrating next generation sequencing (NGS) results, e-medication data and clinical evidence for therapy decision making in adult and paediatric cancers, common and rare. The system will enable user-friendly interpretation and pathogenicity ranking of the NGS variants, according to ACMG/AMP/ASCO/CAP guidelines, using functional and medical annotations through external resources and the Cancer Genome Interpreter (CGI). The CGI identifies potential driver mutations, known mutations and actionable biomarkers. Users will be able to select the relevant variants and the associated information to generate a customisable report for clinicians supporting medical decision-making. The clinical reporting module will support off-line consultation for optimal bedside use. Patients may access a simplified version of the report via a secure mobile app. The reports will be translated into at least 3 languages. The Cancer Reporting GPAP is designed around a well-defined and streamlined workflow, envisioning different types of users, each with specific roles and permissions. The system will be based on the current RD-Connect Genome-Phenome Analysis Platform, developed upon a big data architecture and a user-friendly graphical user interface (GUI), accessible through a web browser. The platform will have a modular design built upon Singularity containers, enabling installation in High Performance Computing clusters and typical Cloud Computing Services. The modular approach will provide flexibility while facilitating updates and backups. Security will be incorporated in all the stages of the Software Development Life Cycle considering the EU GDPR and relevant ISO and IVDR requirements.

Contractor: Congenica L4 (Tender lead: Congenica Ltd)

Congenica's reporting platform provides treatment recommendations as well as information about access to clinical trials for all cancer patients, both adult and children. This information is based on the genetic make-up of each patient and is reported together with additional information about the amount and frequency with which the identified recommended drugs should be taken by the individual. All relevant information about the results and recommendations is initially provided to Physicians and Genetic Counsellors for consultation. However, patients can subsequently request a personalised report, either on paper or via an App, which in an easy-to understand, patient-oriented manner will present the findings together with educational information on, for instance, the value of NGS testing, interaction of medication and support organisations.

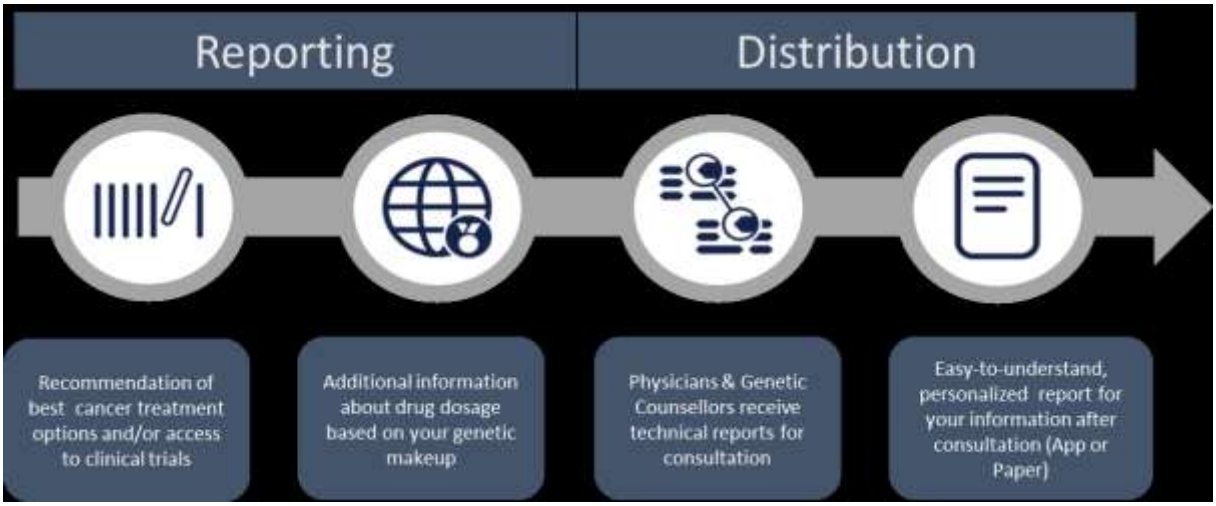

Figure: 1

Finally, Congenica's reporting platform will meet the users' needs listed in the specification, events and findings from Congenica'sresearch. The platform will be integrated with patients' Health Records and will be available in paper, on the patient system or via an App to allow Physicians rapid access to all patient-relevant information and history, whether at a Physician's office, or at the bedside.

Contractor: EU Onco-Platform (Tender lead: BC Platforms AG)

Our consortium is composed of three companies: BC Platforms (BCP), Euformatics (EUF), both with R&D operations in Finland, and Oncompass Medicine (OCM) with R&D operation in Hungary. We address a universal need to generate clinical insights from genomic high throughput (NGS) data in order to facilitate precision / personalised medicine programs. All vendors in the consortium have a well documented background in software development and customer implementations, and can therefore provide enterprise level, user friendly software solutions with adequate expertise in documentation and training activities. All vendors also have experience in molecular pathology reporting and this experience will be most valuable in collaboration with Lot 3 solutions. We plan to develop and add newly developed software modules to our respective existing modular product portfolios, thereby solving NGS4P challenges as well as strengthening our global market impact. This "EU ONCO-PLATFORM" will automate rich annotation and speed up filtering, classification, and interpretation of genomic data by providing innovative methods for identifying the most effective treatment for patients with cancer, based on the complex molecular profile of their tumour. Our capabilities to integrate, automate, version control and enact NGS workflows will ensure high

flexibility. Development on top of award-winning reporting solutions will ensure clinical performance and standardised procedures for decision support, whilst keeping patient perspective, cyber security and regulatory compliance clear throughout development.

Contractor: Tde4ngs (Tender lead: fragmentiX Storage Solutions GmbH)

We have developed the design of a novel, innovative solution that will bring the treatment of cancer to the next level. Each patient will benefit from personalized medicine which is based on determining and analysing the patient's genetic data. The exact genetic information of the patient will be combined with the latest results from medical and pharmaceutical research. Consequently, drug intolerances will be strongly decreased and the search for medication that fits to the patient's conditions will be faster. The patient can leave the hospital earlier and has a better chance of survival. The clinical effort and costs of the treatment will decrease at the same time. The result of the analysis will be immediately available for clinicians in the form of well-structured, detailed reports which show all relevant information. The prescribed medication will fit to the patient's condition and her/his identified genome variants. Patients will get easy-to-comprehend reports. All reports will be available through a web-service, and on apps for mobile devices. The patient's data is well protected against data leakage and data loss using unique secret sharing technologies which remove the need to trust a single data storage provider. The team has been led by fragmentiX Storage Solutions, experts in IT security and privacy protection, supported by medical experts, ID Berlin, experts in software for e-medication including pharmacogenomics, Maxeler Technologies, experts in high performance data processing and data analytics, and Prime-Force experts in document creation, reporting and version management of documents.

Contractor: VRSM (Tender lead: Saphetor SA)

We plan to apply our agile methodology to adapt our existing VarSome Clinical variant interpretation platform to meet purchaser and user expectations. We will focus on augmenting the identification and interpretation of variants found in genes associated with adult and pediatric cancers; producing a sleek reporting interface including pharmacogenomic recommendations; and developing an Application that will help physicians and patients to review genetic reports. VarSome maintains, harmonizes, and integrates over 140 human genomic data sources and over 32 million publications, providing clinicians and researchers the most comprehensive variant interpretation engine available. The power of this database can be demonstrated through over 2 000 peer-reviewed publications in which it has been cited. This is largely due to VarSome's proprietary ACMG (for germline mutations), AMP (for cancer-specific mutations), and CNV (for a specific type of structural variant) classifiers that apply industry standard variant interpretation guidelines to help users interpret their samples quickly and confidently. VarSome is used by over 500 000 users across healthcare, academia, and industry. VarSome's Clinical analysis platform in particular is trusted by over 150 clinical and research institutions around the world. In addition to superior annotation and classification capabilities, VarSome Clinical adheres to strict data This procurement receives funding under the European Union's Horizon 2020 research and innovation programme under the grant agreement No 874719. The EU is however not participating as a contracting authority in this procurement 2 privacy policies, being both HIPPA and GDPR compliant; as well as being one of the first CE-IVD certified tertiary analysis platforms commercially available thanks to being ISO 27001 and ISO 13485 Certified. VarSome Clinical is also expected to be IVDR certified in the coming months to ensure users are compliant within the regulatory environment.