

## Optimal treatment for patients with solid tumours in Europe through Artificial Intelligence

**All information regarding future IMI Call topics is indicative and subject to change. Final information about future IMI Calls will be communicated after approval by the IMI Governing Board.**

### Topic details

Action type	Research and Innovation Action (RIA)
Submission and evaluation process	2 stages
IMI2 Strategic Research Agenda - Axis of Research	Adoption of innovative clinical trial paradigms
IMI2 Strategic Research Agenda - Health Priority	Cancer

### Specific challenges to be addressed by public-private collaborative research

Demands of cancer care in Europe continue to increase significantly, with the number of incident cancer cases in Europe projected to increase by 14.1% by 2030<sup>1</sup>. This leads to a growing demand for innovative cancer treatments among patients, payers, physicians, and society. At the same time, the understanding of the complex biology of cancer is growing, and as a result, pharmaceutical companies are developing a multitude of new therapeutic agents. These include, but are not limited to, novel kinase inhibitors, immunotherapy combinations, and cell therapies.

This trend for new, effective therapies creates more treatment options for patients. However, it confronts physicians with an increasingly expanding number of potential therapeutic options, which each need to be understood and adopted effectively. Numerous factors such as genetic analysis, specific tumour biology, and biomarkers have a growing influence on clinical decision-making. To become familiar with the huge volume of available information, physicians need to learn continuously about medical guideline changes and marketed treatments. In conclusion, future decision-making processes will become ever-more complex, with the potential outcome of sub-optimal or

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<sup>1</sup> <https://gco.iarc.fr/tomorrow/home>

even incorrect treatment choices being made. Furthermore, some patients have disease characteristics for which evidence of guideline recommendations is scarce and physicians lack information about real-world treatment outcomes. Hence, the challenges to be addressed are assisted guideline-based decision-making and the discovery of knowledge about treatment outcomes in real-world settings. As the latter challenge requires analysis of large data sets, the application of Artificial Intelligence (AI) will be a key technology.

To ensure the challenges can be properly addressed, and ensure the innovations reach the physicians and patients, a public-private partnership is necessary, including the following actors:

- **patient organisations and regulatory authorities** to specify the requirements and boundaries of AI-driven data processing, data security and privacy as well as individual data ownership
- **medical societies** to provide the network of participating in- and out-patient clinics to enable data access
- **medical experts/institutions** to specify AI approaches, validate the decision support and set the requirements for general acceptance
- **life-science companies** to contribute study data for the evaluation of therapeutic approaches, as well as expertise in data mining and data-set merging
- **SMEs** for infrastructure set-up, data management and data security, AI-driven data processing and merging of unstructured information, visualisation and user experience design.

## Scope

The scope of this call topic is to establish guideline-based decision support and platform solutions to generate knowledge discovery for breast, lung and prostate cancer with applicability to other indications, in several European (EU member states and H2020 associated countries) 'model' regions. The model regions serve as platforms to show general feasibility of the decision-support tool and lay the foundation for further expansion to other European regions. The results obtained from these model regions are expected to be of relevance to countries with different socioeconomic backgrounds. The funded action will focus only on breast, lung and prostate cancer. These indications show a high number of cases per year, a high, unmet medical need, multiple available therapeutic options and a fast-evolving treatment environment. Expansion to other indications is not part of the funded action but a proposed solution should allow for expansion afterwards. The three core objectives of this call topic are as follows:

### **Objective 1: Establish a guideline-based decision support for prioritised indications**

Development of a decision-support tool that automatically extracts relevant clinical information from electronic health records (EHRs) and facilitates guideline-compliant treatment approaches for the defined solid tumours.

### **Objective 2: Establish a structured and interoperable data platform to unlock real-world-data potential in an oncology network**

A major requirement for the provision of patient-specific treatment is the availability and the harmonisation of extensive patient data across in-patient (e.g. academic centres, teaching hospitals) and out-patient (community and private practices) settings - stored in a structured format, ready to be used and interoperable. The successful consortium should address this need by involving relevant and available regional/national networks of in-/out-patient clinics providing access to their data, for instance with the inclusion of medical societies.

Easy-to-use new platforms that enable the gathering and granular storage of clinical data to offer a foundation for data analysis and knowledge discovery need to be established. The real-world data platforms should include prospective data from electronic health records, structured data from (non)interventional studies provided by members of the pre-identified industry consortium as well as potentially registry data.

### **Objective 3: Leverage the real-world-data gathered by the action to establish an AI-knowledge base and support treatment decisions for prioritized indications**

The funded action will develop a disease-specific (breast, lung and prostate cancer) AI system that facilitates the discovery of novel medical knowledge. This includes hypothesis generation about optimal treatment sequences for patients and prognostic features that can be validated in clinical research. The output will strongly support building the European health data space and improve the quality and acceptance of AI-generated evidence in decision making in research and healthcare delivery. It will also set the foundation for explainable AI approaches necessary for personalised treatment.

During the funded action, members of the industry consortium plan to contribute scientifically relevant pre-existing data and/or data from prospective studies including activities for generating such data that are part of broader industry clinical studies and making such data fit for purpose.

### **Expected key deliverables**

In order to address the call topic challenges, the selected action must ensure that current medical knowledge is quickly translated into clinical practice. It must deal with patients who do not fully match the reasoning paths of guidelines due to certain characteristics for which evidence is limited. Finally, it must be able to decipher how current treatment approaches affect patient outcomes in the real world.

The collaborative public-private consortium is expected to address these challenges in a three-step process. First, a guideline-based decision-making tool that automatically extracts and validates relevant clinical information from EHRs needs to be developed. Second, a database for real-world treatment outcomes needs to be created. Third, AI-technology is to be applied to analyse the data and facilitate novel knowledge discovery.

#### **Overarching considerations:**

- Ensure adherence to existing regulatory guidelines and (e.g. GDPR, Convention on Human Rights and Biomedicine (Oviedo Convention), WMA Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks);
- Patient informed consent for data collection and data sharing;
- Real-world data must be provided from identified countries having access to cancer treatments suggested by treatment guidelines;
- A business model for a platform that is 'sustainable by design' for public health applicability;
- Provision of a detailed concept for its sustainability, maintenance and commercialisation;
- Present concepts and strategies about how their respective proposals will have an impact on competitiveness and industrial leadership of Europe in a sustainable way, e.g. via SME engagement.

#### **A guideline-based decision-support tool:**

- Develop a decision model based on national and/or international clinical guidelines for the three indications; breast, lung and prostate cancer;
- Implement the decision model and integrate into existing IT infrastructures;
- Establish methods to acquire and process decision-relevant clinical information automatically from EHRs;
- Include mechanisms to quickly adapt guideline changes or updates, and scale to incorporate guidelines from additional countries after the project ends.

#### **Data platform:**

- Integration of multi-language user frontends;

- Implementation of secure and interoperable cloud-based data storage;
- Integration into existing clinical IT infrastructures across various geographies to address socioeconomic barriers and IT infrastructure differences;
- Integration of system mechanics that address individual data ownership and transferable data access and usage permissions via extended rights;
- Consideration of different viewpoints on the data based on the stakeholder group:
  - Physicians; a transparent decision-support and intuitive result visualisations;
  - Patients; data ownership and permission management;
  - Patient organisations patient-centric viewpoints;
  - SMEs; programming interfaces.
- Relevant data sources can be derived from electronic health records, (non)Interventional study data or registry data and may include, for example:
  - Patient demographics;
  - Lab panel;
  - Pathological cancer classification;
  - Genomic data;
  - Treatment sequences;
  - Radiology and nuclear medicine reports.
- Documentation of outcomes data like progression-free survival, overall survival, quality of life and adverse events;
- A description of how generated data will be shared with other institutions to further evaluate the generated results and enable transnational comparison throughout the different healthcare systems;
- Applicants are allowed to bring in an existing platform that is then tailored to the needs of the project.

#### **Deliverables of the AI-supported knowledge discovery:**

- Healthcare providers should be able to monitor the impact of the solutions regarding personalised medical treatment as well as the associated cost and outcome;
- Integration of verified knowledge (e.g. outcomes data such as progression-free survival, overall survival, quality of life and adverse events) into the indication-specific knowledge base;
- Process of knowledge discovery needs to be guided by a scientific review committee;
- Consortium members and third parties must be able to request data analyses after approval of the scientific review committee;
- Integration of simulation features based on the knowledge base, e.g. to simulate therapy response, side-effects, quality of life or other outcome-related factors based on prediction modelling on top of the retrospective case data.

#### **Expected impact**

In their proposals, applicants should describe how the outputs of the project will contribute to the following impacts and include wherever possible baseline, targets and metrics to measure impact.

- An explainable AI-based knowledge discovery platform should enable the development of data-driven solutions with the goal to sustainably improve oncologic treatments throughout the EU and beyond;
- The results obtained from these model regions are expected to be of relevance to countries with different socioeconomic backgrounds;

- The platform should allow oncologists to save valuable time due to the automatic data gathering and facilitated guideline-based assessment;
- In addition, physician-patient communication and shared decision making should be supported which might improve proactive therapy involvement to accomplish increases in individual quality of life as well as overall patient satisfaction;
- The platform may also allow research questions from various stakeholders to be answered through data analysis and data pooling as well as data extraction. Besides overall survival, this could include real-world quality of life (QoL) and safety evaluations of new therapies as well as novel combinations under real world conditions. This can potentially contribute to value-based healthcare assessments at EU level;
- The solutions provided by a public-private consortium will significantly benefit European society: patients receive optimal personalised treatment; physicians are supported in complex decision-making processes; and payers as well as pharmaceutical companies receive information about real world treatment outcomes as a foundation for value-based healthcare approaches;
- The topic is well aligned with the EU Commission's strategy to develop a European Health Data Space and Europe's Beating Cancer Plan.

In their proposals, applicants should outline how the project plans to leverage the public-private partnership model to maximise impact on innovation, research & development, as well as regulatory, clinical and healthcare practices, where relevant. This could include a strategy for engagement with patients, healthcare professional associations, healthcare providers, regulators, Health Technology Assessment (HTA) agencies, payers etc., where relevant.

In addition, applicants should describe how the project will impact the competitiveness and growth of companies including SMEs.

In their proposals, applicants should outline how the project will:

- Manage research data including use of data standards<sup>2</sup>;
- Disseminate, exploit, and sustain the project results. This may involve engaging with suitable biological and medical sciences Research Infrastructures<sup>3</sup>;
- Communicate the project activities to relevant target audiences.

## Potential synergies with existing consortia

Synergies and complementarities should be considered with relevant national, European and non-European initiatives (including suitable biological and medical sciences research infrastructures) in order to incorporate past achievements, available data and lessons learnt where possible, thus avoiding unnecessary overlap, and duplication of efforts and funding.

## Industry consortium

The industry consortium is composed of the following EFPIA partners:

- Pfizer (lead)
- Abbvie
- Amgen

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<sup>2</sup> Guidance on data management is available at [http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management\\_en.htm](http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management_en.htm)

<sup>3</sup> <http://www.corbel-project.eu/about-corbel/research-infrastructures.html>

- Bayer
- Roche

The industry consortium plan to contribute the following expertise and assets:

- Personnel with expertise in oncology solid tumours, AI algorithm implementation, real-world data;
- Real-world data from (non)interventional studies supplementing the public partner cohorts. Relevant data may include, for example, outcome results like progression-free survival, overall survival, quality of life and adverse events as well as patient demographics and treatment sequences.

## Indicative duration of the action

The indicative duration of the action is 60 months.

This duration is indicative only. At stage 2, the consortium selected at stage 1 and the predefined industry consortium may jointly agree on a different duration when submitting the stage 2 proposal.

## Indicative budget

The financial contribution from IMI2 JU is a maximum of EUR 10 460 000.

The indicative in-kind contribution from EFPIA partners is EUR 11 400 000.

The EFPIA contribution includes EUR 3 500 000 financial contribution. The allocation of this financial contribution will be decided by the full consortium at stage 2 when preparing the full proposal.

Due to the global nature of the participating industry partners and IMI2 JU Associated Partners, it is anticipated that some elements of the contributions will be non-EU/H2020 Associated Countries in-kind contributions.

## Expertise and resources expected from applicants at stage 1

The stage 1 applicant consortium is expected, in the submitted short proposal, to address all the objectives and key deliverables of the topic, taking into account the expected contribution from the industry consortium which will join at stage 2 to form the full consortium.

The stage 1 submitted short proposals should include suggestions for creating a full proposal architecture which could be in line with the suggested architecture described below, though this architecture is only a suggestion.

**This may require mobilising, as appropriate the following expertise:**

- Expertise in medical oncology with a special focus on the three prioritised indications: breast, lung and prostate cancer;
- Expertise from patient organisations as well as regulatory expertise to address data security and privacy as well as individual data ownership and AI-driven data processing;
- Large-scale medical data management and processing expertise to ensure proper data modelling according to current technical and infrastructural standards;
- Expertise in interoperable IT system design e.g. implementing Health Level 7 Fast Healthcare Interoperability Resources (HL7 FHIR);
- Expertise in technical interface development regarding current clinical technologies and systems such as EHR, Picture Archiving and Communication Systems (PACS) or Laboratory Information Management Systems (LIMS);
- Advanced database and transfer security, client- and server-side encryption (E2E), system threat modelling and prevention;
- User experience design and accessibility considering the broad spectrum of potential users;

- Application development for different server- and client-side systems (e.g. web applications and mobile operating systems);
- Big data analysis;
- Strategies to deal with unstructured data;
- Strategies for handling unfavourable data sets (e.g. incomplete or missing data);
- Methodologies of proper semantic and contextual modelling of patient and disease characteristics;
- Unification, pre-processing, and validation of multimodal clinical data sources.

The size of the consortium should be proportionate to the objectives of the topic while ensuring its manageability.

Furthermore, at stage 1, the applicant consortium should also provide a strategy for allocating the amount of EFPIA Financial contribution – mentioned under indicative budget. The allocation will be decided by the full consortium at stage 2 when preparing the full proposal.

**It may also require mobilising, as appropriate, the following resources:**

Considering the development of AI-supported data analysis and knowledge modelling, applicants will need to provide extended competences regarding:

- Network of clinics (in- and/or out-patient) with access to patient level electronic health records.

**Considerations for the outline of project work plan**

In their stage 1 proposals applicants should:

- Give due visibility on data management, dissemination, exploitation and sustainability, and communication activities. This should include the allocation of enough resources for these tasks which will be further developed in stage 2 proposal;
- Consider including a strategy for ensuring the translation of the projects results to drug development, regulatory/ Health Technology Assessment (HTA) settings (e.g. through scientific advice / qualification advice / opinion, etc.), clinical and healthcare practices, and/or decision-making processes.

**Suggested architecture**

The project challenges are summarized in Figure 1.



### Work package 1 – Project management

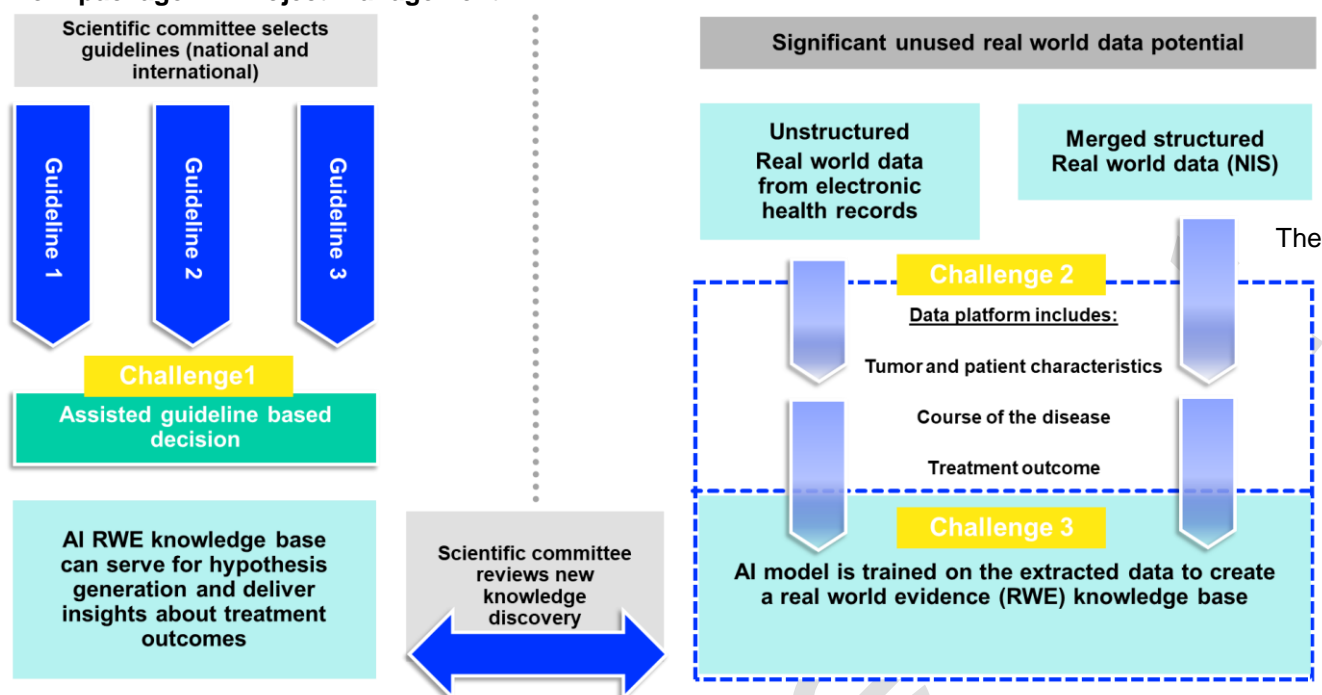


Figure 1 – Overview of project challenges.

goals of this work package are to:

- Ensure alignment between the beneficiaries as well as smooth internal and external communication;
- Monitor compliance with the work plan;
- Monitor planned resources and time schedule;
- Coordinate fulfilment of all administrative milestones;
- Ensure legal and data privacy requirements are met during the project lifetime.

**The expected applicant consortium contribution should include** project management, ensuring the implementation of the coordinating tasks and running the day-to-day operation, such as project tracking and reporting, meetings, internal communication, website creation, budget management, etc.

### Work package 2 – Informed consent, general requirement analysis, governance, and regulation

The goals of this work package are to:

- Obtain patient informed consent;
- Technical and medical requirement analyses to specify the clinical need and required technical infrastructure;
- Design of governance principles for both data platform and AI component including legal structures in participating countries and sites;
- Definition of ethical principles towards the application of AI in a medical context;
- Conceptualisation of long-term operation and monetisation strategies;
- Requirements for data privacy adherence (e.g. GDPR).

### Work package 3 – Guideline-based decision support tool



The goals of this work package are:

- Identification of relevant treatment guidelines for the targeted indications by a scientific committee;
- Development of model-based representations of those guidelines;
- Allowing instantiation of the decision models with real-world patient data;
- Integration of automatic reasoning methods for the individual patient case;
- Integration of an automatic or assisted evaluation pipeline for model updates and adjustments.

#### **Work package 4 – Platform technical and infrastructural requirement analysis**

The goals of this work package are:

- Specification of the technical platform infrastructure;
- Consideration of necessary tools for data analysis and knowledge discovery;
- Specification of all necessary technical interfaces;
- Evaluation of data storage and management strategies;
- Establishment of a resource plan including strategies for resource scaling;
- Development of a data and operations security framework.

#### **Work package 5 – Platform implementation and evaluation**

The goals of this work package are:

- Generation of user personas based on the relevant platform stakeholders;
- Integration of data analysis tools or integration of compatibility features for external applications;
- Development of automated testing and deployment pipelines;
- Conduction of a user study to evaluate visual and functional platform components accordingly to the generated personas;
- Platform and interface documentation for users and third-party developers.

#### **Work package 6 – (Non)interventional study data and real-world data gathering, preparation and integration**

The goals of this work package are:

- Aggregation and evaluation of available study data sources;
- Consideration of all legal and ethical aspects relating to the data sets;
- Assessment of gathered data pools regarding quality and impact of the contained data;
- Quality assurance in terms of data preparation;
- Establishment of a processing pipeline for unstructured entities;
- Strategies to deal with inconsistent or missing information.

#### **Work package 7 – Artificial Intelligence knowledge base implementation**

The goals of this work package are:

- Development of a suitable knowledge representation scheme;
- Development of pre-processing features for data integration (e.g. validation);

- Integration of explainability and traceability mechanisms that allow for linking individual discoveries to the respective evidence and its derivation;
- Integration of system-assisted validation features for a committee of experts (e.g. peer-review) that verifies individual findings before knowledge base integration.

## Work package 8 – Dissemination and communication

## Work package 9 – Exploitation and sustainability of the results

### Additional considerations to be taken into account at the stage 2 full proposal

At stage 2, the consortium selected at stage 1 and the predefined industry consortium jointly submit the full proposal developed in partnership. The full proposal is based upon the selected short proposal at stage 1.

In the spirit of the partnership, and to reflect how IMI2 JU call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, these beneficiaries intend to significantly contribute to the programme and project leadership as well as project financial management. The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 JU rules and with a view to the achievement of the project objectives. The allocation of a leading role within the consortium will be discussed in the course of the drafting of the full proposal to be submitted at stage 2. To facilitate the formation of the final consortium, until the roles are formally appointed through the consortium agreement, the proposed project leader from among EFPIA beneficiaries/large industrial beneficiaries shall facilitate an efficient negotiation of project content and required agreements. All beneficiaries are encouraged to discuss the project architecture and governance and the weighting of responsibilities and priorities therein.

#### Data Management

In their stage 2 proposal, applicants should give due visibility to data management including use of data standards. A full 'data management plan' (DMP) as a distinct deliverable must be delivered within the first 6 months of the project. The DMP needs to be kept up to date with the needs of the project and as such be **updated as necessary during its lifetime**.<sup>4</sup>

#### Dissemination, exploitation and sustainability of results

In their stage 2 proposal, applicants must provide a draft plan for dissemination and the exploitation, including sustainability of results. A full plan as a distinct deliverable must be delivered within the first 6 months of the project<sup>5</sup>, and updated during the project lifetime and could include identification of:

- Different types of exploitable results;
- Potential end-users of the results;
- Results that may need sustainability and proposed sustainability roadmap solutions.

Sufficient resources should be foreseen for activities related to dissemination and exploitation, including the plan for the sustainability of the project results. This may involve engaging with suitable biological and medical sciences Research Infrastructures (RIs).<sup>6</sup>

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<sup>4</sup> Guidance on data management is available at [http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management\\_en.htm](http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/open-access-data-management/data-management_en.htm)

<sup>5</sup> As an additional dissemination obligation under Article 29.1 of the [IMI2 Grant Agreement](#) will apply.

<sup>6</sup> <http://www.corbel-project.eu/about-corbel/research-infrastructures.html>

### **Communication**

The proposed communication measures for promoting the project and its findings during the period of the grant should also be described and could include a possible public event to showcase the results of the project.

Indicative text