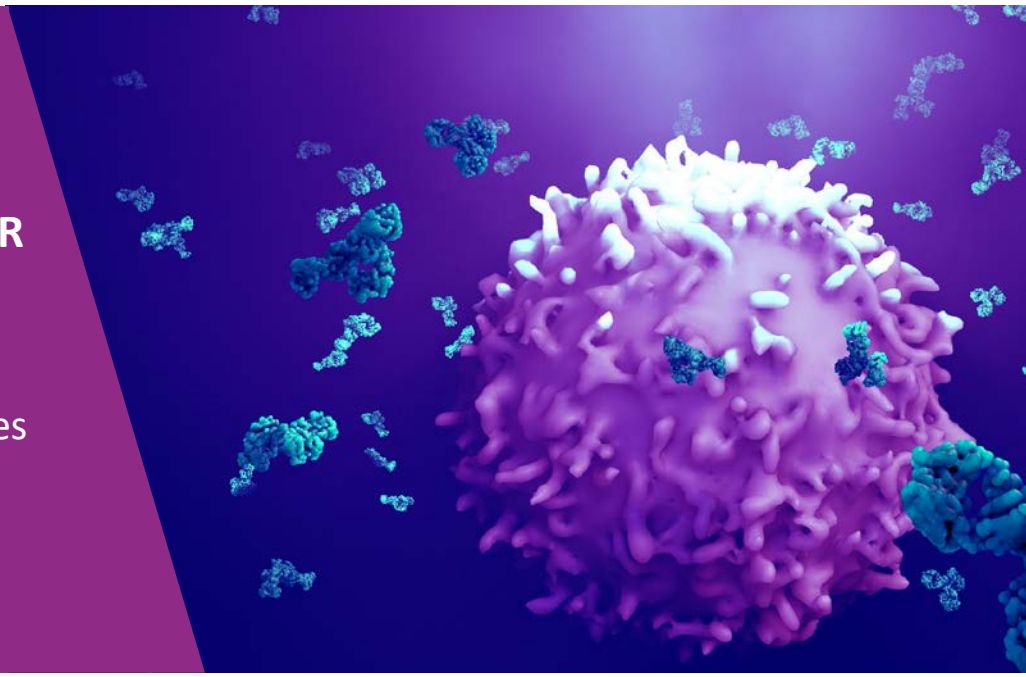
imSAVAR

IMMUNE SAFETY AVATAR

Nonclinical mimicking of the immune system effects of immunomodulatory therapies



Deliverable 1.12
Involvement of Regulatory Agencies

DELIVERABLE REPORT

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 853988.
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innovative medicines initiative

efpia

JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Abstract

The responsibility for engaging with regulatory agencies within imSAVAR falls into work package 1: Management, task 1.3 Stakeholder Engagement. The Deliverable 1.12, was implemented in the 4th Amendment upon request from the reviewers. The imSAVAR project aims to deliver a range of tools that will enhance the ability to assess the efficacy and safety of immunomodulatory therapies with regards to immune oncology and immune inflammatory diseases. The preclinical evaluation of such novel immunotherapies in terms of efficacy and safety remains a significant challenge, primarily due to the intricate nature of the human immune system itself and its altered functions in diseased states. One tool is to define immune-related adverse outcome pathways (irAOPs) to describe bio-logical effects triggered by an initiating event leading to adverse health effects of new thera-pies. In regards of regulatory aspects it is important to get feedback on these tools early enough whether they are appropriate and will get approval from the EMA and FDA as a standard approach out of imSAVAR. A white paper about this defined irAOPs is currently under preparation and will serve as a discussion basis for further and deeper exchange with the regulatory board and ultimately regulatory agencies. Irrespective of this, imSAVAR has been in contact with experts who are experienced in regulatory matters since the start of the project.

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1. Importance of Regulatory Advice

To facilitate the translation of new tools and methodologies into health products and to guide regulatory decisions that benefit patients, it is crucial that consortia are well-versed in the regulatory framework and key requirements. This knowledge will enhance the likelihood that research findings later will be transformed into innovative solutions that meet regulatory standards, gain regulatory approval, and can then be adopted by other researchers or developers, ultimately reaching patients. Additionally, this will help to raise the profile of research outcomes and contribute to their long-term sustainability. For example, if a new method has received regulatory qualification from the European Medicines Agency (EMA) and/or US Food and Drug Administration (FDA), it indicates that the method is deemed acceptable from a regulatory standpoint for use in a specific research and development context (known as the "context of use") based on a thorough evaluation of the scientific evidence provided. Since the qualification opinion is made publicly available, this method can be applied by other researchers or developers within the specified context as they work on healthcare products, and it can be integrated into regulatory assessments. Therefore, it is crucial to involve individuals with regulatory experience early in the project to gather their feedback and benefit from their knowledge. In 2024 the European Commission published a guide for regulatory considerations for IMI/IHI projects to raise awareness and give some advice how to address this in EU projects.[1]

2. imSAVAR Regulatory Advisory Board

Regulatory experts in imSAVAR are involved via a regulatory advisory board. The criteria for eligibility, selection process and their role have been laid down in the project's description and consortium agreement. The Regulatory Board shall consist of no more than 7 members. Nominations for membership of the Regulatory Board may be submitted to the Project Integration Team by any Beneficiary. The Project Integration Team shall ensure that the composition of the Regulatory Board is appropriate to provide the guidance required to achieve Action goals and shall invite nominees to the Regulatory Board accordingly. Members of the Regulatory Board shall be approved by the Steering Committee. Prior to their first participation in a meeting of the Regulatory Board or their first receipt of Confidential Information, any Third Party expert or qualified person shall first enter into a suitable Advisory Agreement. The Regulatory Board is an advisory board to the Action in general and the Steering Committee and Project Integration Team in particular. The Regulatory Board will advise the Steering Committee and the Project Integration Team upon the request of the Project Leader together with the coordinator and provide non-binding advice to the Steering Committee and the Project Integration Team as decision making support.

3. Involvement of Regulatory Advisory Board

The regulatory advisory board was invited to attend imSAVAR's 5th consortium meeting in October 2023. Their participation was more specifically foreseen for the presentation on the "Gender dimension in manifestation of immune-related adverse events" by imSAVAR member C. Sakellariou (University of Lund). After this talk, which had been based on literature research, the results of the Study-a-thon conducted in June 2023 and the active participation and exchange with our patient stakeholder community and consortium partners shared some insightful questions that were then addressed in our internal work package meetings. These fruitful discussions enabled the consortium partners to further work on defining and developing the models. In order to engage more and request feedback from

[1] Guide_RegulatoryConsiderationsIMI_IHI_Projects_final.pdf (europa.eu)

regulatory agencies, a White Paper about the irAOPs defined in imSAVAR is being prepared. The white paper will give an overview of irAOPs, demonstrate their value, and delineate the challenge of modelling the immune sys-tem. Use cases for irAOPs will also be outlined. The authors will include a section with a list of questions intended for regulatory experts. This document will be part of a briefing book that we will share with the European medicines Agency's (EMA) Innovation Task Force (ITF) in the context of our request for a briefing meet-ing. These meetings assist developers in deciding on next steps in their development pro-grammes with regards to regulatory, technical and scientific concerns arising from innovative medicines, technologies and methodologies. Briefing meetings are an informal exchange of information and guidance in the development process, complementing existing formal EMA procedures.[2]

4. Challenges

From the start of the project, we have been searching for external regulatory experts to join the imSAVAR Regulatory advisory Board. However, the task proved to be complex. We invited eight experts from different institutions but only received two positive answers. This low rate of acceptance is mainly due to the lack of time of the contacted experts and difficulties in negotiating the Agreements because of extensive confidentiality provisions. Most of the people asked have already been involved in several other projects. We consequently established a regulatory board consisting of two members: Dr. Gabriele Reichmann from the Paul-Ehrlich Institute and Dr. Carmen Sanges from the University of Würzburg. Nevertheless, we have recently reached out to two additional experts who have shown interest in becoming involved in imSAVAR's Regulatory Board. Furthermore, it took a long time to establish a mutual understanding regarding the involvement of regulatory experts. This was also due to the fact that it was only later in the project that results were available for which regulatory feedback was relevant.

5. Conclusion

One of the aims of imSAVAR is to bring a degree of harmonisation and alignment to the process of immune safety assessment. It is therefore important that we engage with diverse stakeholders. To achieve that aim we need to be able to establish a participatory community that will continue to update and extend our efforts. It is also of critical importance that we gather stakeholder input to inform the effort to refine and develop the irAOPs, and models. This is particularly important in terms of regulatory advice. To achieve this goal, we have planned a process that is centred around workshops, formal regulator advice, and meaningful patient stakeholder involvement. Despite challenges in recruiting external regulatory experts, the imSAVAR consortium has established a regulatory advisory board and has recently invited two additional experts. Meetings have been held with experts before and during imSAVAR's 5th consortium meeting, which has enabled our partners to consider new venues of reflection and the defining and development of models. The next phase will see a deepening of our effort to engage with regulatory agencies with the preparation of a White Paper highlighting the role and value of irAOPs. This document, which will be part of a briefing book, will be discussed and finalized during an upcoming workshop with our regulatory advisory board. Thereafter the imSAVAR consortium will share the briefing book with the European medicines Agency's (EMA) Innovation Task Force (ITF) with the purpose to request a briefing meeting.

[2] Supporting innovation | European Medicines Agency (EMA) (europa.eu)

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