Executive Summary
3rd Project Period

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101007757
The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Context and Objectives

The overall objective of the HIPPOCRATES project is to lead to significant improvements in people living with psoriatic arthritis (PsA) outcomes. We aim to do this by addressing four key areas of unmet needs for people with psoriatic disease. Our main objectives are to find and develop biomarkers and clinical tools for: i) improved (early) diagnosis of Psoriatic arthritis (PsA), ii) the evaluation of the risk of progression from psoriasis to PsA, iii) identification of those for whom structural damage and functional decline is rapid, and iv) predicting response to main PsA therapies The project comprises eight interconnected work packages (WPs) that embed and involve patients, clinicians, primary care practitioners, regulators, SMEs, and five relevant pharmaceutical company partners. Together these WPs will: i) combine the most extensive and well-studied cohorts of patients with psoriatic disease across Europe to establish and maintain a Europe-wide library of clinical biosamples and associated data; ii) discover, evaluate, and validate biomarker signatures that address the key unmet needs in psoriatic disease; and evaluate biomarker signatures to develop diagnostic algorithms/tools for clinical implementation. Through four 'data gathering' WPs we will identify clinical and molecular markers and in a fifth 'big data' WP (WP5) will combine the data and analyse it using advanced artificial intelligence strategies. The planning and progress of HIPPOCRATES is managed and coordinated at multiple levels and include meticulous and continuous review of ethical considerations. A separate WP is devoted to communicating the activities of HIPPOCRATES and includes the development of a strategy for project sustainability.

Partners

UNIVERSITY COLLEGE DUBLIN, NATIONAL UNIVERSITY OF IRELAND, DUBLIN (Coordinator) - UNIVERSITY OF GLASGOW - UNIVERSITATSKLINIKUM ERLANGEN - VIB VZW - FRAUNHOFER GESELLSCHAFT ZUR FOERDERUNG DER ANGEWANDTEN FORSCHUNG E.V. - KATHOLIEKE UNIVERSITEIT LEUVEN - THE UNIVERSITY OF MANCHESTER - THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD - ATTUROS LIMITED - EURICE EUROPEAN RESEARCH AND PROJECT OFFICE GMBH - FUNDACIO CLINIC PER A LA RECERCA BIOMEDICA - RIGSHOSPITALET COPENHAGEN - UNIVERSITA CATTOLICA DEL SACRO CUORE - GRAPPA-EU - STICHTING GROUP FOR RESEARCH AND ASSESSMENT OF PSORIASIS AND PSORIATIC ARTHRITIS EU - EUROPEAN LEAGUE AGAINST RHEUMATISM - SIB INSTITUT SUISSE DE BIOINFORMATIQUE - THE EUROPEAN INSTITUTE FOR INNOVATION THROUGH HEALTH DATA - STICHTING AMSTERDAM UMC - OXFORD BIODYNAMICS LIMITED - KUNGLIGA TEKNISKA HOEGSKOLAN - KING'S COLLEGE LONDON - NOVARTIS PHARMA AG - UCB BIOPHARMA SRL - BRISTOL-MYERS SQUIBB COMPANY CORP - PFIZER LIMITED - Trajan Scientific Europe Ltd - AbbVie Inc

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101007757.
The JU recieves support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Scientific Results

In year 1 of HIPPOCRATES much of our effort was devoted to establishing the WP teams and consortium building. We've used a few innovative methods to build the teams including a 'team book' and tokens of recognition for exemplary individual contributions. Each of the four 'data gathering' WP teams (WP1-4) established detailed plans for prioritising sample cohorts and accessing samples including and identifying what data and analyses will be collected. Three cross-WP working groups covering Clinical Data Harmonisation (CDH), Imaging and Biomarkers supported these activities.

In year 1, the initial discussions on the development of a HIPPOCRATES Data Sharing Agreement (DSA) began and included representatives of WPs 1-4 with significant contributions from the legal teams in UCD, the EFPIA partners, the Swiss Institute of Bioinformatics and the Fraunhofer. The DSA was signed by all partners in Oct 2023, and this represented a major achievement as it permitted consolidation of all HIPPOCRATES clinical and molecular data into a central database (the Secure HIPPOCRATES Data Management Platform (SHDMP) hosted at the Swiss Institute of Bioinformatics) with access to the data for all HIPPOCRATES partners. The DSA is supported by a consortium-wide Material Transfer Agreement to enable the sharing of biological samples. At the end of period 3, data from 7 cohorts, totalling 2284 patients, including 4 omics datasets have been uploaded to the SHDMP with plans to have all prioritised cohorts uploaded before the end of 2024.

Most cohorts to be included within HIPPOCRATES are retrospective (already collected), but we have now made significant progress with recruiting participants to the HIPPOCRATES Prospective Observational Study (HPOS) which is part of WP2 on predicting Pso-PsA conversion. The study was launched in the UK and Ireland in Q3 2023, and Greece and Portugal in Q2, 2024. The study has been rolled-out to up to 15 other EU countries by the end of 2024. By June 2024, more than 3,000 people with psoriasis had been recruited.

Within WP2, a pilot study to identify molecular factors which may predict the development of PsA in people with psoriasis has been completed. Serum samples from people with psoriasis and no features of PsA, samples from people with psoriasis and perhaps some early PsA features as well as samples from people with established PsA (30 subjects in each group) were shared with 5 centres (UGLA, UMAN, KTH, FhG-CIMD and Atturos). Each centre analysed the samples and conducted initial data analysis. These study results were presented as an oral abstract at Europe's main Rheumatology congress, 2024. Now that all these data are uploaded to the SHDMP and shared with data analysts at the Fraunhofer, combined machine learning and artificial intelligence approaches to data analysis is underway. All of this initial work will

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101007757.
The JU recieves support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

inform the best approach to be taken when combining molecular/clinical data generated in other WPs

As noted, 3 working groups have been established to facilitate cross-WP efforts related to CDH, Imaging, and Biomarkers. The working groups have each made substantial progress. Within the CDH working group, data managers from all HIPPOCRATES partners who are providing cohort data to the consortium (WP1-4) met bi-weekly and a HIPPOCRATES Glossary Expert group has developed a PsA glossary. To harmonize the glossary, these meetings have included input from the IMI BIOMAP team.

The Biomarker working group (with representatives from WP1-5) have mapped the detailed logistics for the planned multi-omic studies including sample types and volumes required as well as requirements for sample collection, processing, and storage. The focus of the Imaging Working group (involving mainly representatives from WP1 and WP3) has been on the identification of cohorts with imaging data and the collection of imaging metadata. This work is now completed and the Imaging working group has merged with the Biomarker working group. The HIPPOCRATES Website is 'active' as are the Twitter and LinkedIn accounts. A communication Toolkit with resources has been developed. In total, there have been 33 peer reviewed publications and 39 presentations (https://www.hippocrates-imi.eu/publications).

Expected final results and impact

By addressing the key areas of unmet needs in PsA and doing so in a coordinated and integrated manner we expect that HIPPOCRATES will lead to the development of diagnostic algorithm(s) for use in primary care settings, as well as in dermatology and rheumatology clinics. We will identify combined clinical and molecular markers for disease progression from skin psoriasis to PsA for further evaluation in HPOS and other large datasets.

Finally, we expect to have further defined the molecular profiles underlying treatment response or non-response in PsA, and to have identified markers of rapid structural damage progression. Together these will support an era of precision medicine in PsA which will have considerable patient, societal and economic benefits.

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101007757.
The JU recieves support from the European Union's Horizon 2020 research and innovation programme and EFPIA.