# A Global, Molecular Disease Characterization Initiative (MDCI) in Oncology Clinical Trials

**Poster No. 390**


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## Background

As of October 2021, there are currently **24,368** ongoing clinical trials for cancer (ClinicalTrials.gov).

- Meta-analysis data have previously shown that often only **8%** of eligible patients participate in clinical trials.[1]

Increasing participant access to potentially life-saving clinical trials has become more complex with the growing clinical interest in precision medicine and biomarker-focused treatment strategies.[2]

- As such, new approaches to clinical trial design are needed to ensure that participants can be quickly and appropriately identified for enrollment into potentially life-saving trials.
  - For instance, the Lung Cancer Master Protocol trial demonstrated the effectiveness of using master protocols to accelerate the development of biomarker-driven therapies.[3]

The **Molecular Disease Characterization Initiative (MDCI)** proposes a solution to the challenge of integrating precision medicine into the participant treatment journey, by:

- Rapidly pre-screening participants for multiple studies at the same time, thereby accelerating the availability of new therapeutic options.
- Evaluating participants' tumor and blood genetics during pre-screening to build a scientific database and facilitate the investigation of biological mechanisms underpinning clinical outcomes.

## Aim

To evaluate molecular and immunological profiles of tumor and peripheral blood in potential participants for clinical trials across cancer indications and within tumor subsets, and to build a GlaxoSmithKline (GSK) Clinical Science Database for tumor profiling and correlative studies.

## Methods

Multicenter study

Single-arm

This study (GSK213299; NCT04772053) will enroll participants with advanced/metastatic malignancies including non-small cell lung cancer (NSCLC).

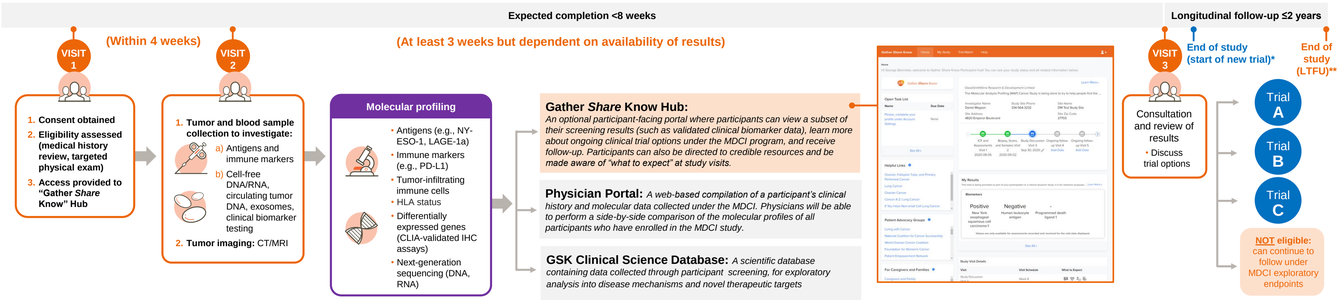
## Study Design

**The MDCI will be an optional protocol under select GSK oncology protocols.**

**Approximately 400 participants** will be enrolled in this molecular analysis study.

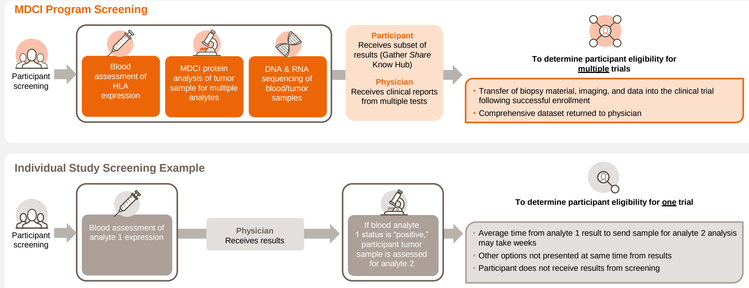
Potential clinical trial options are sent to both physicians and participants based on molecular profiling results and the participant's previous medical history, with the aim of reducing time-to-treatment.

## Study Design




* "End of study" here is defined per protocol as when a participant consents to enroll onto a GSK or other clinical study; ** "End of study" here is defined per protocol as after 2 years of longitudinal follow-up. CLIA, Clinical Laboratory Improvement Amendments; CT, computed tomography; HLA, human leukocyte antigen; IHC, immunohistochemistry; LAGE-1a, cancer testis antigen 2; LTFU, longitudinal follow-up; MDCI, Molecular Disease Characterization Initiative; MRI, magnetic resonance imaging; NY-ESO-1, New York esophageal squamous cell carcinoma 1; PD-L1, programmed death ligand-1.

### Participant flow example illustrating reduced time-to-treatment and increased participant access to trials under the MDCI program




MDCI, Molecular Disease Characterization Initiative.

Participants may be subsequently matched to ongoing clinical trials within a GSK study spanning different therapeutic modalities **(Table 1).**

Immuno-oncology

Cell and Gene Therapy

Synthetic Lethality

Each of these platforms provides the opportunity for a precision medicine approach using agents (such as small molecules, engineered immune cells, or poly [ADP-ribose] polymerase inhibitors) that target tumor-specific biomarkers, alone or in combination with other therapies.

Participants who do not match to a clinical trial but continue with standard of care may choose longitudinal follow-up and further analysis of their disease at time of progression.

### Table 1. Current GSK clinical studies* associated with the MDCI program

| NCT Number | Study Title |
|---|---|
| NCT03739710 | A Phase II, Randomized, Open-label Platform Trial Utilizing a Master Protocol to Study Novel Regimens Versus Standard of Care Treatment in NSCLC Participants |
| NCT04475939 | A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study Comparing Niraparib Plus Pembrolizumab Versus Placebo Plus Pembrolizumab as Maintenance Therapy in Participants Whose Disease Has Remained Stable or Responded to First-Line Platinum-Based Chemotherapy With Pembrolizumab for Stage IIIB/IIIC or IV Non-Small Cell Lung Cancer (ZEAL-1L) |
| NCT03709706 | A Phase 1b/2a Pilot Study to Evaluate the Safety and Tolerability of Autologous T-Cells Expressing Enhanced TCRs Specific for NY-ESO-1/LAGE-1a (GSK3377794) Alone, or in Combination With Pembrolizumab in HLA-A2+ Participants With NY-ESO-1- or LAGE-1a-Positive Advanced or Recurrent Non-Small Cell Lung Cancer |
| NCT04526509 | Master Protocol to Assess the Safety and Recommended Phase 2 Dose of Next Generations of Autologous Enhanced NY-ESO-1/LAGE-1a TCR Engineered T-cells, Alone or in Combination With Other Agents, in Participants With Advanced Tumors |
| NCT04655976 | A Randomized, Open-Label Phase 2/3 Study Comparing Cobolimab + Dostarlimab + Docetaxel To Dostarlimab + Docetaxel To Docetaxel Alone In Participants With Advanced Non-Small Cell Lung Cancer Who Have Progressed On Prior Anti-PD-(L)1 Therapy And Chemotherapy (COSTAR Lung) |
| NCT04446351 | A Phase 1 First-Time-in-Human, Open-Label Study of GSK6097608 Administered as Monotherapy and in Combination With Anticancer Agents in Participants With Advanced Solid Tumors |

*Studies listed are as of October 11, 2021, and include additional studies with ongoing activity. MDCI sites are among the first to be assessed for feasibility for hosting new studies or ongoing studies expanding at the site. The MDCI study will screen participants only where the GSK treatment protocol has incorporated MDCI language that is approved at the site.

HLA, human leukocyte antigen; LAGE-1a, cancer testis antigen 2; MDCI, Molecular Disease Characterization Initiative; NCT, National Clinical Trial Number; NSCLC, non-small cell lung cancer; NY-ESO-1, New York esophageal squamous cell carcinoma 1; PD-(L)1, programmed death ligand-1; TCR, T-cell receptor.

## Eligibility Criteria

**Key inclusion criteria:**

Confirmed advanced/metastatic diagnosis of solid malignancy (including but not limited to NSCLC, head and neck squamous cell carcinomas, breast, ovarian, colorectal); life expectancy of >6 months; ability to provide blood samples.

**Key exclusion criteria:**

ECOG performance >2; history of myocardial infarction, acute inflammatory heart disease, unstable angina, or uncontrolled arrhythmia within the past 6 months; for female participants, pregnancy; any serious and/or unstable pre-existing medical, psychiatric disorder, or other condition that could compromise safety, compliance, or obtaining informed consent.

## Endpoints

**Primary Endpoint:**

- To profile participant-specific selection biomarkers that can be targeted by therapeutics within GSK oncology clinical trials under the MDCI program.

**Exploratory Endpoints**

- Evaluate participant usage in the participant hub
- Collect & correlate sociodemographic & clinical outcomes
- Identify new biomarkers
- Examine molecular profiling & imaging
- Assess overall safety (adverse events and serious adverse events related to study procedures)

## Summary


This study will involve multiple sites, located over a wide geographic footprint globally, with the intention of significantly expanding opportunities for molecular identification profiling of participants and easing the current screening process.

This is expected to help advance the matching of participants to trials and expedite time-to-treatment in precision medicine trials.

The MDCI is expected to benefit numerous groups:

**Participants** will be screened under **one** trial for several clinical trials without the need for sequential rounds of biomarker characterization or biopsy sampling, when applicable. This is expected to increase participant convenience and improve the time between diagnosis and treatment. Additionally, plain-language summaries of participant test results will improve participants' understanding of their disease and options for treatment.

**Physicians** will be provided with a full comprehensive view of sequencing, biomarker, and disease status of participants with a reduced volume of repetitive participant diagnostics.

**Oncology researchers** will benefit with facilitation of innovation and further understanding of mechanisms of action or resistance; the data collected will provide a robust dataset and data for training artificial intelligence and machine learning algorithms that could provide new insights into the mechanisms and treatment of cancer.


## Expected Impact of MDCI Model

The MDCI aims to create a platform to accelerate the availability of new therapeutic options for participants and increase participation in precision medicine clinical trials, while building the GSK Clinical Science Database to facilitate the further investigation of biological mechanisms underpinning clinical outcomes in oncology.


**Disclosures**

**MLJ** receives or has received research funding to their institution from AbbVie, Acerta, Adaptimmune, Amgen, Apexigen, Arcus Biosciences, Array BioPharma, Artios Pharma, AstraZeneca, Atreca, BeiGene, BerGenBio, BioAtla, Boehringer Ingelheim, Calithera Biosciences, Checkpoint Therapeutics, Corvus Pharmaceuticals, Curis, CytomX, Daiichi Sankyo, Dracen Pharmaceuticals, Dynavax, Lilly, Elicio Therapeutic, EMD Serono, Erasca, Genentech/Roche, Genmab, Genocea Biosciences, GlaxoSmithKline (GSK), Gritstone Oncology, Guardant Health, Harpoon, Helsinn Healthcare SA, Hengrui Therapeutics, Hutchison MediPharma, IDEAYA Biosciences, IGM Biosciences, Immunocore, Incyte, Janssen, Jounce Therapeutics, Kadmon Pharmaceuticals, Loxo Oncology, Lycera, Memorial Sloan-Kettering, Merck, Mirati Therapeutics, NeoImmune Tech, Neovia Oncology, Novartis, Numab Therapeutics, OncoMed Pharmaceuticals, Pfizer, PMV Pharmaceuticals, RasCal Therapeutics, Regeneron Pharmaceuticals, Relay Therapeutics, Revolution Medicines, Ribon Therapeutics, Rubius Therapeutics, Sanofi, Seven and Eight Biopharmaceuticals / Birdie Biopharmaceuticals, Shattuck Labs, Silicon Therapeutics, Stem CentRx, Syndax Pharmaceuticals, Takeda Pharmaceuticals, Tarveda, TCR2 Therapeutics, Tempest Therapeutics, Tizona Therapeutics, TMUNITY Therapeutics, Turning Point Therapeutics, University of Michigan, Vyriad, WindMIL, Y-mAbs Therapeutics; 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and has participated on a safety review committee for Adaptimmune and GSK. **HZ** has previously received a research contract from Checkmate Pharmaceuticals and consulting fees from Vedanta and iTeos. **JW** consults for and has received less than $10,000 dollars per annum from Merck, Genentech, AstraZeneca, GSK, Novartis, Nektar, Celldex, Incyte, Biond, ImCheck, Sellas, Evaxion, and EMD Serono and $10–25,000 dollars from BMS for membership on advisory boards; holds equity in Biond, Evaxion, Instil Bio, OncoC4, and Neximmune; on scientific advisory boards for Evaxion, ImCheck, Biond, Sellas, Instil Bio, OncoC4, and Neximmune, and is remunerated $10,000–$75,000; is not a member of any speaker's bureau; New York University, but not JW personally, received research support from BMS, Merck, GSK, Moderna, Pfizer, Novartis, and AstraZeneca; named on an ipilimumab biomarker patent and on TIL preparation patent filed by Moffitt Cancer Center, and named on a PD-1 patent filed by Biodesix; receives less $1500 yearly in royalties. **EBG** reports consulting or advisory roles for ABL Bio, Boehringer Ingelheim, Bristol Myers Squibb, Dracen Pharmaceuticals, Eisai, Eli Lilly, EMD Serono, GSK, Merck, Natera, Novartis, Regeneron, Sanofi, Shionogi, and Xilio Therapeutics; 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a non-executive director and shareholder of TCR2 Therapeutics; a board of trustees member of the Sabin Vaccine Institute; a non-executive director and shareholder of Imugene; and a co-chair of the steering committee for the Cancer Research Institute, Cancer Immunotherapy Consortium.



**Acknowledgments**

We would like to acknowledge John Yonchuk for his contributions to this work. We wish to thank our technical and laboratory partners for their support with developing this program. This study is funded by GlaxoSmithKline (Study 213299; NCT04772053). Editorial support was provided by Eithne Maguire, PhD, of Fishawack Indicia, part of Fishawack Health, and funded by GSK.



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**Presented at the Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting & Pre-Conference Programs | November 10–14, 2021**