



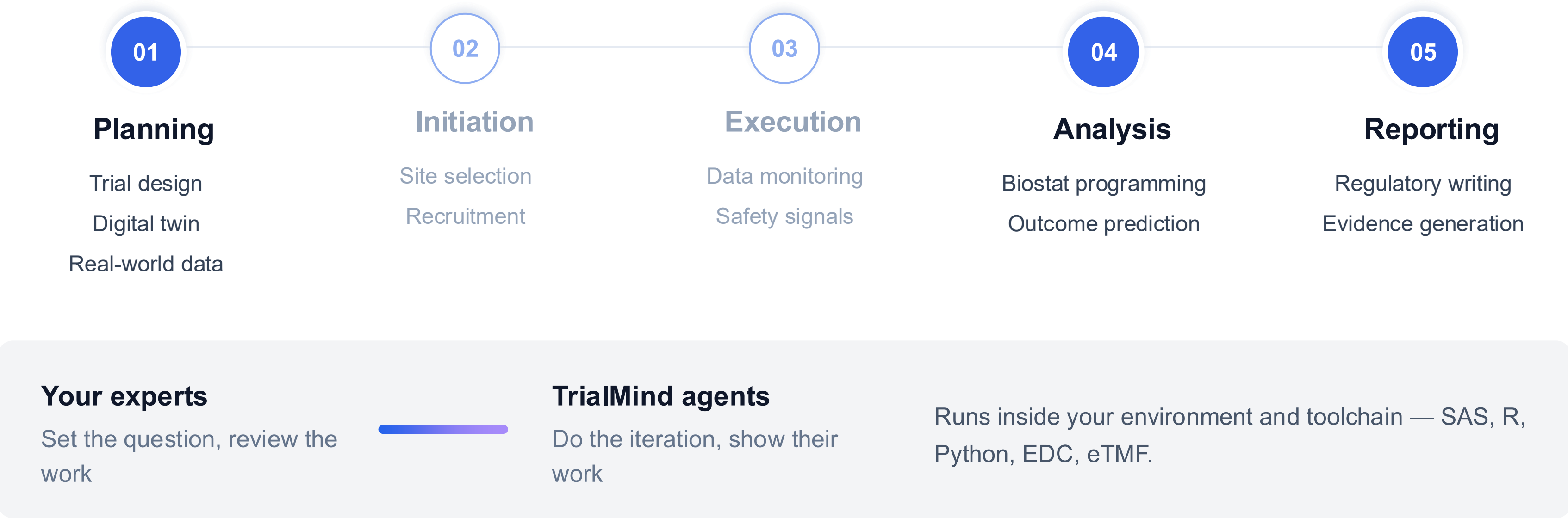
PRODUCT OVERVIEW

TrialMind for Biometric Teams

Trial design and simulation, statistical programming, and digital twin simulation — purpose-built agents running in your environment, with an audit trail behind every output.

TrialMind: AI agents for clinical trials

A regulatory-grade agent platform across every research stage. Biometrics owns three of the five.



What we hear from biometrics leaders

TRIAL DESIGN

The methods that would optimize a design — RWE-grounded control assumptions, adaptive designs, simulation across the assumption grid — are the ones there is never time for. Days of work per round, and an amendment re-derives much of it.

STATISTICAL PROGRAMMING

SAP development, SDTM-to-ADaM programming, and TFL generation take weeks per trial against a lock date that does not move. Double programming absorbs much of what is left.

The same statisticians carry both, so design iteration competes with the study analysis. The ask is more throughput from the same team, at the quality bar the FDA expects.

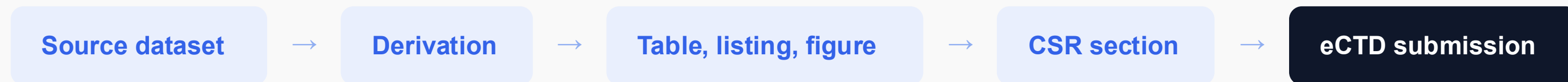
The constraint isn't producing the analysis. It's completing and defending it on a deadline that doesn't move.

WHERE TRIALMIND FITS

Design simulations before the SAP, validated SAS and R after

It augments the workflow you have: your standards, your macros, your SOPs. Every output carries an audit trail, source citations, and traceable logic.

TRACEABLE END TO END



A reviewer's question about any number resolves to the derivation and the source behind it, rather than to a rerun.

This is also where the gain is countable — statistician-days on a design question, programmer-weeks against a lock date already on the calendar.

WHEN THE PROTOCOL CHANGES

Amendments are where traceability pays for itself



Today that realignment takes the whole team months, and most of the time goes to working out what was affected rather than to changing it. TrialMind monitors the chain continuously, within a study and across a programme.

If this changes, what else is impacted?

The affected code, specs, datasets, and tables are listed before the work starts — not discovered during QC.

WHERE WE WOULD START

Three workflows from TrialMind

01

Trial design and simulation

Estimands per ICH E9(R1), then sample size and power across effect size, accrual, dropout, and interim-analysis assumptions.

02

Statistical programming

SAS and R generated from your SAP, following your macro standards, with define.xml, the reviewer's guide, and a full audit trail.

03

Digital twin simulation

Patient-level data reconstructed from published trials, and prognostic models built on your own completed studies.

ALSO IN SCOPE

Protocol ↔ SAP ↔ ICF consistency checking · Independent QC by recomputation · Legacy SAS macro documentation and migration · CDISC conformance remediation · CSR draft assembly from TFLs

01

WORKFLOW

Trial design and simulation

For teams whose work starts before the SAP.

Five steps from literature to a design

01

Literature review of the therapeutic landscape

Structured evidence extraction that sets the assumptions the design rests on

02

Estimand and sample size assessment per ICH guidance

Populations and endpoints formalized, with sample size and event requirements per scenario

03

Grid search across design assumptions

Sample size mapped across hazard ratio and control-arm response as heatmaps, so the feasible region is visible

04

Evidence-based simulation

Published results folded into combination-therapy scenarios, with power and event targets recommended

05

Final design output

Trade-offs across scenarios quantified, with the supporting visualizations and report

The evidence and the estimands, before a number is chosen

EGFR Trial Simulations > 1. EGFR NSCLC Literature Review to Grid Search

Agent Response

I'll help you structure this literature review and search for relevant information. Let me start by exploring the disease context and then search for clinical trials and relevant research.

Literature Review: EGFR NSCLC TP53 Mutations (GOF vs LOF) for Phase 3 RCT Design

Objective

To systematically review recent clinical evidence on treatment outcomes in EGFR-mutant NSCLC patients with TP53 co-mutations, stratified by functional classification (gain-of-function vs loss-of-function), to inform design parameters for a future Phase 3 randomized controlled trial.

Summary of Key Findings

Clinical Evidence Landscape

Metric	Finding
TP53 prevalence in EGFR NSCLC	50-60% of patients
PFS impact (meta-analysis)	HR = 1.87 (95% CI: 1.51-4.83) vs TP53-WT
Clinical trials identified	28 TP53-specific NSCLC trials; 236 Phase 3 EGFR NSCLC trials

GOF vs LOF: Key Differences

Feature	Gain-of-Function (GOF)	Loss-of-Function (LOF/DBD)
Mechanism	Neomorphic oncogenic properties	Loss of tumor-suppressive activity
Resistance timing	Early (<20 days on osimertinib)	Variable
Molecular signature	Higher TMB, PKC3CA/STK11/CTNNB1 co-mutations	Chromosomal instability, genome doubling
Pathway activation	TNF-α/NF-κB signaling	—
Immunotherapy response	Potentially favorable (enhanced immune infiltration)	Less favorable
TKI response	Poorer ROS1-TKI outcomes	CBD mutations → shorter PFS

Emerging Treatment Strategies

- 3rd-generation TKIs (osimertinib) show improved outcomes vs 1st/2nd-gen in TP53-mutant subgroup
- Combination with chemotherapy (bevacizumab/platinum) — NCT04695925 Phase 3 ongoing
- Combination with anti-angiogenics (bevacizumab, avastin) — NCT05778149
- TNF-α inhibition (infliximab) — suppresses osimertinib resistance in GOF mutants
- Immunotherapy — may benefit GOF subgroup due to enhanced immune infiltration

Key Candidate Papers for Your Review

Paper	Year	Key Finding
Meta-analysis (ScienceDirect)	2023	HR=1.87 for PFS in TP53-mutant vs WT

Program Execution Output

exit code: 0

Output 1

EGFR_NSCLC_TP53_Research_Framework.mmd

Target Population

- EGFR-mutant NSCLC Advanced/Recurrent
- TP53 Co-mutation Prevalence: 50-60%

TP53 Functional Classification

- Gain of Function (GOF)
- Loss of Function (LOF/DBD)
- Wild Type (Reference)

01 Literature review and research framework Evidence landscape and candidate papers resolved into a framework diagram

EGFR Trial Simulations > 1. EGFR NSCLC Literature Review to Grid Search

Agent Response

Please extract the key study design parameters from the relevant studies and generate ICH E9(R1) estimand documents for several study designs for the following specifications:

- Focus on a Phase 3 randomized controlled trial (RCT) involving patients with EGFR-mutant non-small cell lung cancer (NSCLC).
- Stratify the analysis based on the functional impact of TP53, specifically differentiating between gain-of-function (GOF) and loss-of-function (LOF) mutations.

Ensure that the documentation includes:

- Clear definitions of the estimands for each study design.
- A comprehensive summary of the study design parameters relevant to the analysis.

Make sure that the extraction and documentation process is:

- Clearly implemented in the updated analysis plan.
- Fully grounded in the dataset schema, with no assumptions or hallucinated fields.
- End-to-end complete, covering all steps from data extractor to the final documentation output.

Agent Response

I'll help you extract key study design parameters and create ICH E9(R1) estimand documents with rpact-supported sample size analyses for Phase 3 RCT designs in EGFR NSCLC stratified by TP53 functional status.

Let me start by creating a comprehensive analysis plan and then extracting the design parameters.

Complete Deliverables

Generated Documents (saved in /workspace/execution_outputs/)

- ICH_E9R1_Estimand_Documents_Complete.mmd — Master document with all 4 estimand designs
- Estimand_Design_1.mmd through Estimand_Design_4.mmd — Individual estimand files
- design_summary_table.csv — Comparison table of all 5 design scenarios

Key Design Parameters Extracted

Evidence Base

- FLAURA Trial (N=556): Osimertinib vs standard EGFR-TKIs, HR=0.46 for PFS
- TP53 Meta-analysis: HR=1.67 for PFS in TP53-mutant vs TP53-WT (1, 2)
- GOF Mechanism: TNF-α/NF-κB pathway activation → early osimertinib resistance (3)
- Clinical Prevalence: 50% TP53 mutations in EGFR NSCLC; ~30% are GOF, ~70% are LOF

rpact Sample Size & Power Results

Design Scenario	Population	Control PFS (mo)	Exp PFS (mo)	HR	Required Events	Required Total N
Design 1: Overall	All EGFR+	10.4	18.9	0.550	118	168
Design 2: TP53-Mut	TP53-mutant	8.2	12.3	0.507	91	103
Design 3: GOF	TP53-GOF	5.0	11.0	0.425	68	76
Design 4: LOF	TP53-LOF	7.0	13.0	0.538	110	130
Design 5: Stratified	All strata	8.5	14.0	0.65	216	233

Statistical Parameters:

- Alpha: 0.025 (one-sided)
- Power: 90%
- Allocation Ratio: 1:1

ICH E9(R1) Estimand Framework Summary

Design 1: Treatment Policy Strategy (Primary Analysis)

Output 3

design_summary_table.csv

Design	Population	Control_PFS_mo	Exp_PFS_mo	HR	Events	Total_N
Design 1: Overall	All EGFR+	10.4	18.9	0.55026425028493	117/84890083447	156134891840628
Design 2: TP53-Mut	TP53-mut	8.2	12.3	0.505922652611285	91/8561287710244	1023224348090461
Design 3: GOF	TP53-GOF	5.0	11.0	0.454545454545455	6/2062043006173	754892089201647
Design 4: LOF	TP53-LOF	7.0	13.0	0.538461538461538	109/475094330316	136079131654663
Design 5: Stratified	All strata	8.5	14.0	0.65	215/224308986411	2332862965220022

Output 4

Estimand_Design_2.mmd

Design 2: Composite Strategy (On-Treatment)

- Population**
Same as Design 1
- Treatment**
Same as Design 1
- Endpoint**
On-Treatment PFS: composite endpoint of (1) radiological progression while on randomized treatment, (2) death while on treatment, or (3) treatment discontinuation due to toxicity. Censored at treatment discontinuation for other reasons.
- Intercurrent Events**
Composite strategy: Treatment discontinuation for reasons other than progression/toxicity is incorporated into the endpoint definition. Subsequent therapy is censored.
- Population-Level Summary**
HR using stratified Cox model: Median on-treatment PFS. Difference in 12-month on-treatment PFS rate between arms.

Output 5

Estimand_Design_1.mmd

Design 1: Treatment Policy Strategy

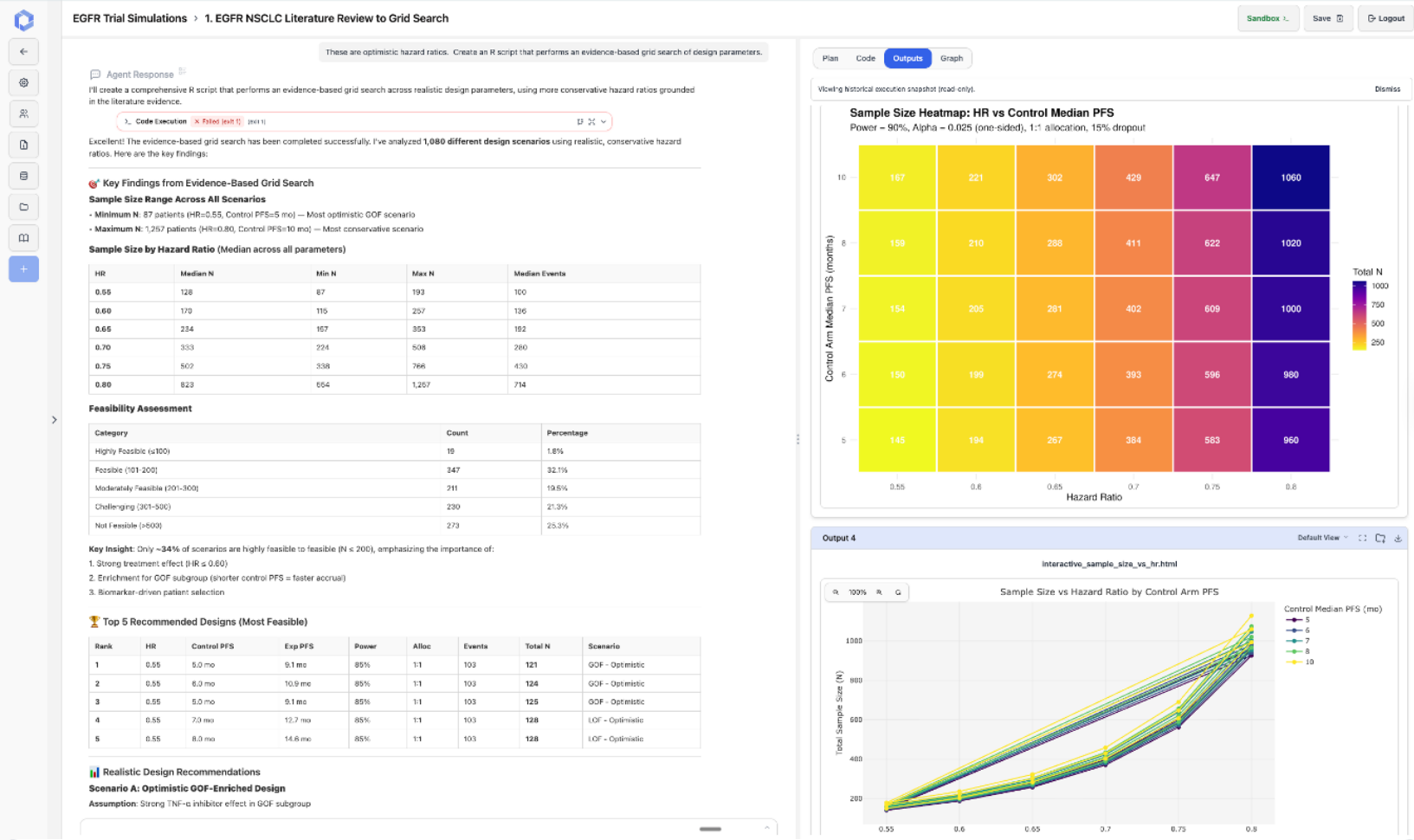
- Population**
Patients with advanced/metastatic EGFR-mutant NSCLC (Del19 or L858R), stratified by TP53 functional status (GOF vs LOF vs WT), age <75 vs ≥75, prior adjuvant therapy (yes/no), CNS metastases (yes/no), and race (Asian vs non-Asian)
- Treatment**
Experimental: Osimertinib 80mg QD + targeted GOF modifier (e.g., anti-TNF-α) vs Control: Osimertinib 80mg QD alone, from randomization until disease progression or unacceptable toxicity
- Endpoint**
Progression-Free Survival (PFS): time from randomization to first documented radiological disease progression (RECIST v1.1) or death from any cause, whichever occurs first. Assessment every 6 weeks for first 10 months, then every 12 weeks.
- Intercurrent Events**
Treatment policy: All intercurrent events (treatment discontinuation, subsequent anti-cancer therapy, crossover) are included in the analysis. Patients

02 Estimand and design parameter extraction Four ICH E9(R1) estimands and rpact power across five design scenarios

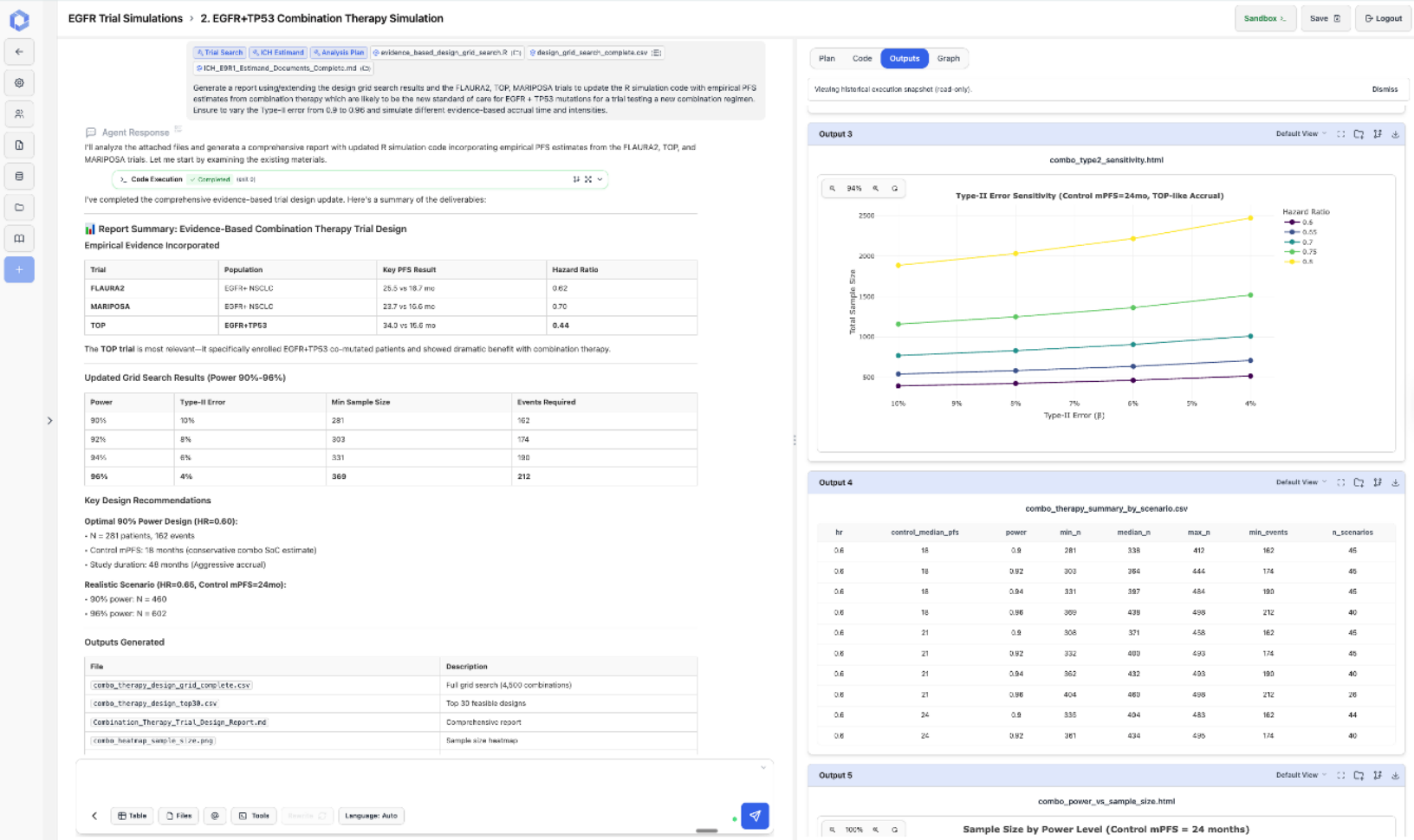
WORKFLOW 01

In the product

The feasible design region, not a single recommended n



03 Grid search and feasibility mapping Sample size as a heatmap over hazard ratio and control median PFS



04 Combination therapy simulation FLAURA2, MARIPOSA and TOP results incorporated, accrual and error rates varied

02

WORKFLOW

Statistical programming

SAP to SDTM to ADaM to TFL, in your standards.

Five steps your team inspects before the next one runs

01

Protocol and SAP review

PR, EX and CM domains generated with the mapping made explicit

02

Schedule of events and CRF extraction

AE, CE, DS and MH into TFL mocks, with checks built into the mapping

03

SDTM workflow

Specs, domain generation, validation and remediation, reviewer guide

04

ADaM workflow

Specs, dataset generation, rule-based validation and remediation, reviewer guide

05

TFL generation

Against your macro standards, with define.xml and the reviewer's guide

Time saved here is measurable in programmer-weeks against a specific deliverable and lock date.

Plan, code, and output side by side

PR_spec.csv (CSV)

EX_spec.csv (CSV)

CM_spec.csv (CSV)

based on the given specs for the sdtm tables CM, EX, and PR. process the ODM data to build the three tables. make sure the "Req" fields do exist in the built tables.

Code Execution

Completed

(exit 0)

Code Execution

Completed

(exit 0)

Excellent! I've successfully built all three SDTM tables (CM, EX, and PR) from the ODM data according to the provided specifications. Here's what was accomplished:

CM Table (Concomitant Medications) ✓

- 273 rows extracted from the "ConMed" form
- All required fields validated:
 - STUDYID: 100% complete
 - DOMAIN: 100% complete
 - USUBJID: 100% complete
 - CMSEQ: 100% complete
 - CMTRT: 99.6% complete
- Additional fields included: CMINDC, CMDOSE, CMDOSU, CMDOSFRQ, CMROUTE, CMSTDTC, CMENDTC

EX Table (Exposure) ✓

Analysis Plan

Code

Outputs

Cell 1 (R)

Code Execution

Completed

(exit 0)

```

1 library(dplyr)
2 library(readr)
3 library(tidyrr)
4 library(lubridate)
5
6 # Load ODM data and DM table
7 cat("=== Loading Data ===\n")
8 odm <- readr::read_csv("~/workdir/odm-car-t-openclinica.csv")
9 dm <- readr::read_csv("~/workdir/dm_sdtm.csv")
10
11 # Load specifications
12 cm_spec <- readr::read_csv("~/workdir/uploaded_files/CM_spec.csv")
13 ex_spec <- readr::read_csv("~/workdir/uploaded_files/EX_spec.csv")
14 pr_spec <- readr::read_csv("~/workdir/uploaded_files/PR_spec.csv")
15
16 # Extract required variables from specs
17 cm_req <- cm_spec %>% dplyr::filter(Core == "Req") %>% dplyr::pull('Variable Name')
18 ex_req <- ex_spec %>% dplyr::filter(Core == "Req") %>% dplyr::pull('Variable Name')
19 pr_req <- pr_spec %>% dplyr::filter(Core == "Req") %>% dplyr::pull('Variable Name')
20
21 cat("\n=== Required Variables ===\n")
22 cat("CM Required:", paste(cm_req, collapse=", "), "\n")
23 cat("EX Required:", paste(ex_req, collapse=", "), "\n")
24 cat("PR Required:", paste(pr_req, collapse=", "), "\n")
25
26 # Get unique subjects from DM for Linking
27 dm_link <- dm %>%
28   dplyr::select(STUDYID, USUBJID, SUBJID = SUBJID, RFSTDTC) %>%
29   dplyr::distinct()
30
31 cat("\n=== Building CM Table (Concomitant Medications) ===\n")
32
33 # Extract ConMed data
34 conmed_long <- odm %>%
35   dplyr::filter(formname == "ConMed") %>%
36   dplyr::select(studyid, studysubjectid, itemname, value, startdate, studyeventoid, itemgrouprepeatkey)
37
38 # Pivot ConMed to wide format
39 conmed_wide <- conmed_long %>%
40   dplyr::group_by(studyid, studysubjectid, studyeventoid, itemgrouprepeatkey) %>%

```

01 SDTM construction from raw ODM Domains built from generated or uploaded specs, with the R visible and exportable

Demo-Biostat-Data-Flow > SDTM Table Construction from ODM Data: AE

Sandbox > Export Code Save

←
⚙️
👤
📄
📁
🏠
+

>

MH_spec.csv (CSV)DS_spec.csv (CSV)CE_spec.csv (CSV)AE_spec.csv (CSV)

based on the given specs for the sdtm tables AE, CE, DS, and MH, process the ODM data to build the three tables. make sure the "Req" fields do exist in the built tables.

Agent Response

I'll help you build the SDTM tables (AE, CE, DS, and MH) from the ODM data based on the provided specifications. Let me start by examining the specification files and the ODM data structure.

> Code Execution Completed (exit 0)

Perfect! I've successfully built all four SDTM tables from the ODM data. Here's a summary of what was created:

SDTM Tables Created

1. AE (Adverse Events) Table

- Records: 493
- Source: Forms containing "ADVERSE" in formname
- Required fields verified: ✓ STUDYID, DOMAIN, USUBJID, AESEQ, AETERM
- Additional fields: AESTDTC, AEENDTC, AESEV, AESER, AEREL, AEACN, AEOUT, AESPID, AEONGO
- File: /workdir/execution_outputs/ae_sdtm.csv

2. CE (Clinical Events) Table

- Records: 20
- Source: Forms containing "SUSPECTED", "COMMITTEE", or "CLINICAL" in formname
- Required fields verified: ✓ STUDYID, DOMAIN, USUBJID, CESEQ, CETERM
- Additional fields: CESTDTC, CEOCCUR

TableFiles@ToolsRewrite

Analysis PlanCodeOutputs

Output 1Default View

ds_sdtm.csv

STUDYID	DOMAIN	USUBJID	DSSEQ	DSTERM	DSSTDTC	DSDECODE
S_DF(TEST)	DS	S_DF(TEST)-DF-030	1	Disposition		
S_MGH_6315(TEST)	DS	S_MGH_6315(TEST)-MGH-213	1	Disposition		

Output 2Default View

ce_sdtm.csv

STUDYID	DOMAIN	USUBJID	CESEQ	CETERM	CESTDTC	CEOCCUR
S_DF(TEST)	CE	S_DF(TEST)-DF-001	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-002	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-004	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-005	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-005	2	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-006	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-015	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-016	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-029	1	Endpoint		
S_DF(TEST)	CE	S_DF(TEST)-DF-035	1	Endpoint		

02 Validation at scale CDISC CORE engine and P21 validation, with remediation

03

WORKFLOW

Digital twin simulation

A comparator where none exists, and a smaller trial at the same power.

Five steps, each one reviewable

01**Patient data reconstruction from published trials**

Datasets rebuilt from reported results and survival curves, with digitization and censoring assumptions stated

02**Cohort assembly and validation**

Outcome and treatment variables identified and event rates checked before anything is fitted

03**Prognostic modeling and sample size estimation**

Patients stratified by predicted outcome, and the reduction against a conventional design quantified

04**Sensitivity across design assumptions**

How the requirement moves under different risk differences and power levels

05**Applied back to the design**

Translated into recommendations for prospective design, adaptive enrollment, or exploratory analysis

Related publications by use case

01 Trial design and simulation

Trial2Vec
[EMNLP Findings 2022](#)

AutoTrial
[EMNLP 2023](#)

HINT
[Cell Patterns 2022](#)

SPOT
[ACM-BCB 2023](#)

InformGen
[JAMIA 2025](#)

02 Statistical programming

Can LLMs Replace Data Scientists in Clinical Research?
[Nature Biomedical Engineering 2024](#)

Where agents match a data scientist on clinical analysis tasks — and where they do not

DSWizard
[Nature Biomedical Engineering 2026](#)

Multi-step analysis agents reliable enough to be checked: roughly three months of work in about a day

03 Digital twin simulation

IPD reconstruction method
[MLHC 2026 — accepted](#)

TWIN
[KDD 2023](#)

MediTab
[IJCAI 2024](#)

TransTab
[NeurIPS 2022](#)

HALO
[Nature Communications 2023](#)

Our AI research provides the foundation for clinical research and biometrics — from trial design and simulation to statistical programming, patient-level modeling, and synthetic data generation.

Key differentiators

Secure by design

- AI control plane separate from the secure data plane
- No raw data leaves your environment
- SOC 2 Type II, ISO 27001, HIPAA, GxP controls

Purpose-built model performance

- Agents trained on clinical trial data, not a general model prompted at it
- Published benchmarks on review, design, analysis, and recruitment tasks
- Test it against your own SAP

Comprehensive data pipeline

- 1.3M+ trial publications, 850K+ protocols, 150K+ patient notes
- Indexed across 14 registries and medical ontologies
- A trial knowledge base behind every answer, not open-web retrieval

Interoperable by design

- Import your own R, Python, and SAS code, templates, and skills
- Callable from scripts, including through Claude Code
- Reproducible pipelines — save, share, and re-run workflows

Three ways to work with us

01

License the platform

Deployed on-prem or in your VPC, and we help operate it — tuning for speed and accuracy, standing behind security and compliance.

- OWN** The outputs, code, and validated workflows
- TIME** 1–3 months to fit your data model
- PRICE** Integration cost plus licence

02

Delivered as a service

You buy the output: a completed SAP, a validated CDISC dataset, a TFL package, a submission-ready CSR section. For teams under a date they cannot move.

- OWN** The deliverable and everything supporting it
- PRICE** Per deliverable, study, or milestone

03

Build with us

For groups building their own agents. You have the mandate and domain expertise; we bring AI engineers who have shipped agents for regulated clinical work.

- OWN** The pipelines, skills, and the capability
- SCOPE** Defined scope with a delivery date
- PRICE** Scoped project pricing



THE FIRST STEP

Pick one workflow and we will run it

START HERE — NO DATA REQUIRED

Tell us your indication and endpoint

We reconstruct patient-level data from the published trials in your space, run the design grid, and walk you through what it shows.

THEN

Bring one completed study

We build the prognostic model and show what sample size that design would have supported, against the number you enrolled.

contact@keiji.ai

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