A prospective master protocol / platform to conduct international multicentric single-arm studies in ultra-rare sarcomas including real world data for external comparisons

Lorenzo D'Ambrosio – University of Turin / AOU San Luigi Gonzaga

Gauthier Bouche – AntiCancer Fund

Rosalba Miceli – Fondazione IRCCS Istituto Nazionale dei Tumori, Milano

COIs*

Lorenzo D'Ambrosio

- Advisory Board: PSI CRO Italy, GSK, AstraZeneca, Boehringer Ingelheim, Eisai
- Meeting participation: GSK, AstraZeneca, PharmaMar

Gauthier Bouche

- No COIs

Rosalba Miceli

- Honoraria: Boehringer Ingelheim (consultancy activities)

*last 3 years

The aim

Maximize the knowledge from every single ultra-rare sarcoma patient to support developing new treatments and improve outcomes and quality of life

The start

RARITY & HETEROGENEITY

Limited
preclinical / clinical / epidemiological
data

R unfeasible

Lower level
of the available evidence

Larger degree of uncertainty
in clinical decision

Inconsistency
in pt care and
Pt discrimination

Few treatments available

Off-label

Less actractive
for the industry
(expecially for agents
already approved in other indications)

Less funding

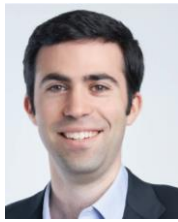
Regulatory issues

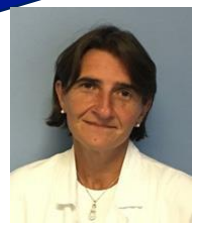
Few (sponsored) clinical studies

Few approved drugs

A global need

















patients

MDs

Research funders

TRs

Biostatisticians

Research Groups

Regulatory Agencies

THE FOUNDATION

CHORDOMA FOUNDATION

CDRC
CURE DRUG REPURPOSING COLLABORATORY

Anticancer Fund

EORTC
European Organisation for Research and Treatment of Cancer

Ultra-rare Sarcoma Working Group

EUROPEAN MEDICINES AGENCY

U.S. FOOD & DRUG ADMINISTRATION

From PUSH To PUSH-IT

PUSH PLATFORM

Pushing Ultra-rare Sarcomas towards Hope

EORTC European Organisation for Research and Treatment of Cancer

Ultra-rare Sarcoma Working Group

CDRC CURE DRUG REPURPOSING COLLABORATORY

UNIVERSITÀ DI TORINO

FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI

Anticancer Fund

THE ECHE FOUNDATION

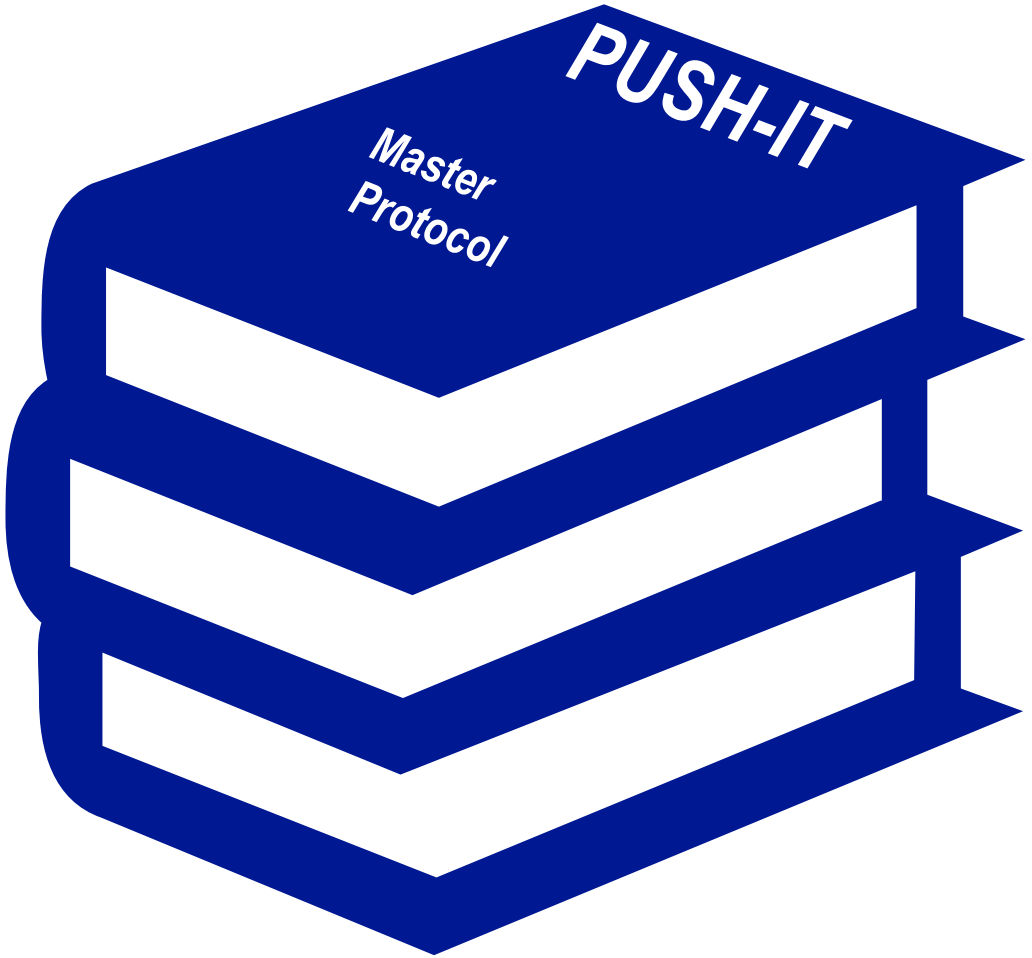
CHORDOMA FOUNDATION

PUSH-IT

Pushing Ultra-rare Sarcomas towards Hope an International Trial

PLATFORM STUDY

Architecture



Master protocol

Common framework / Governance

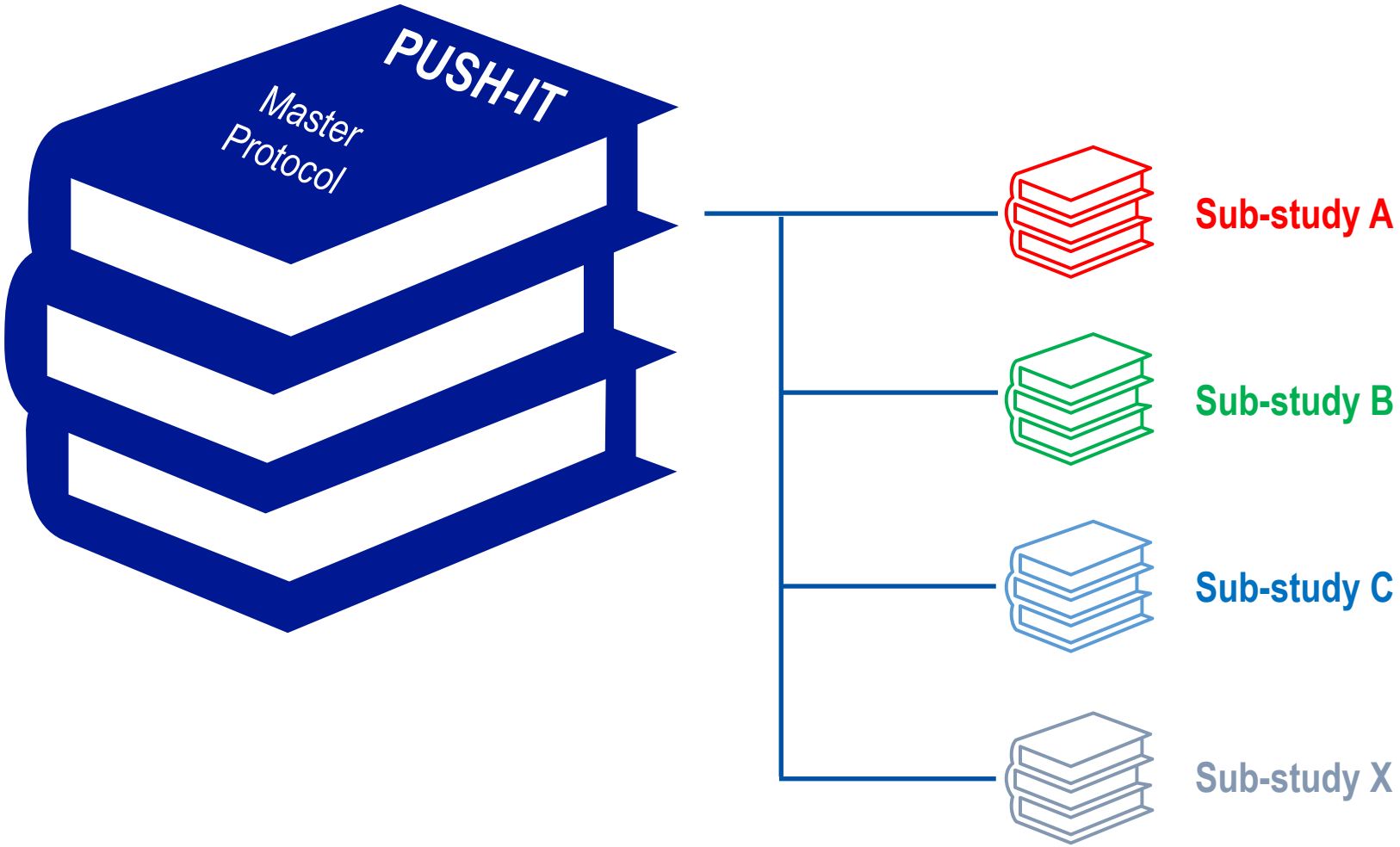
Pre-defined design hypotheses

Ethics

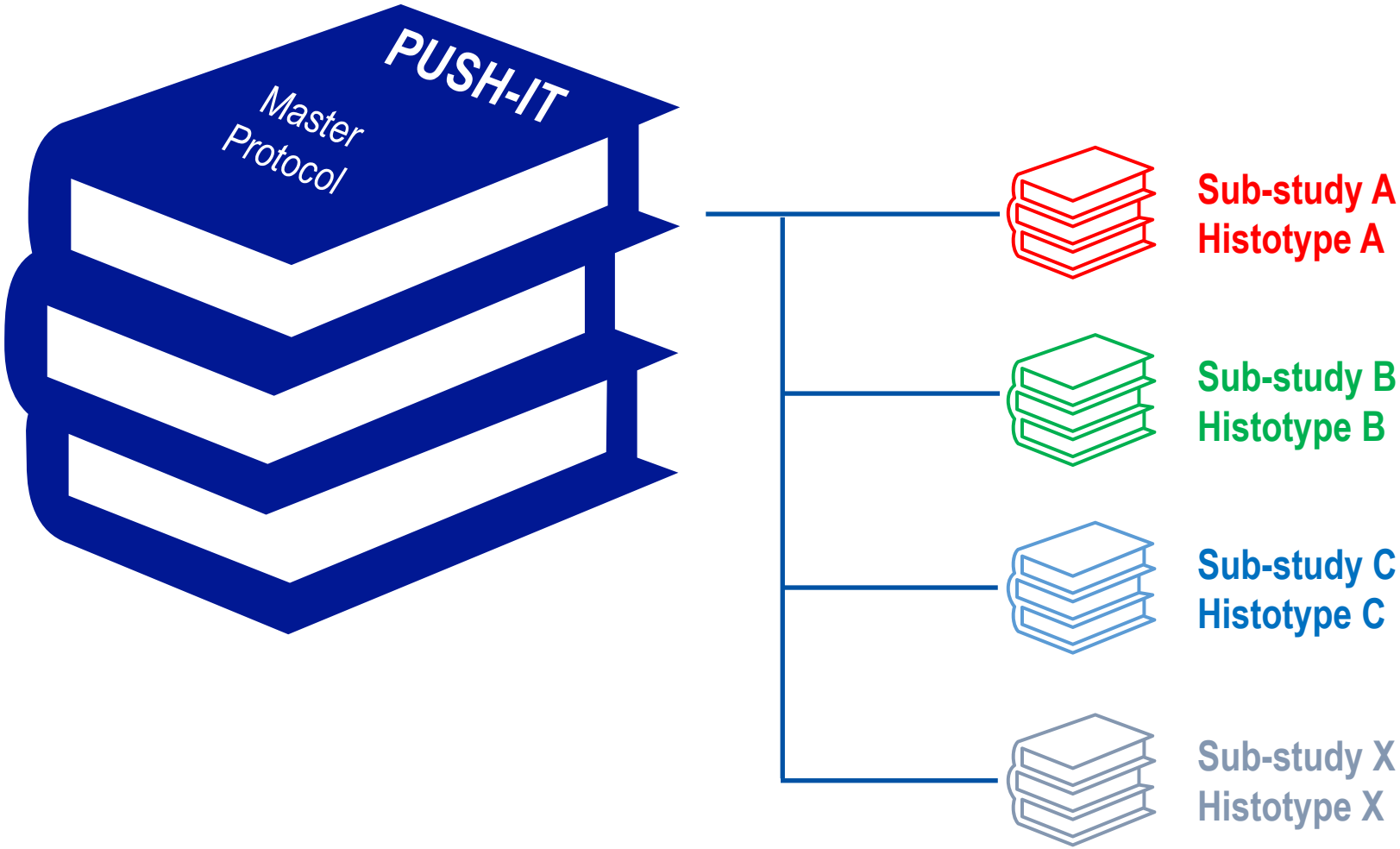
Data management

IT

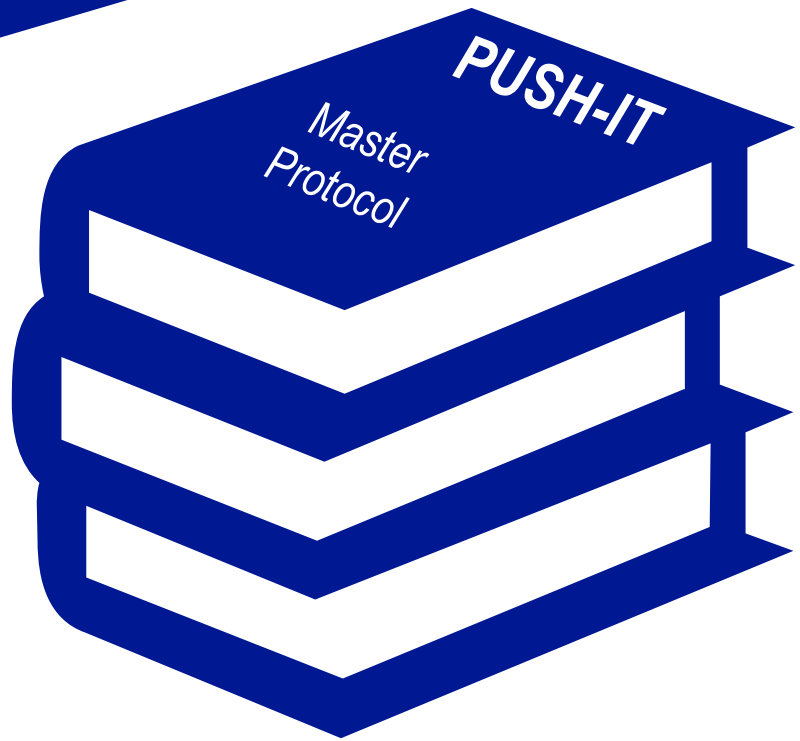
Sub-studies

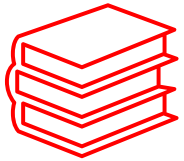


Sub-studies



Single arm

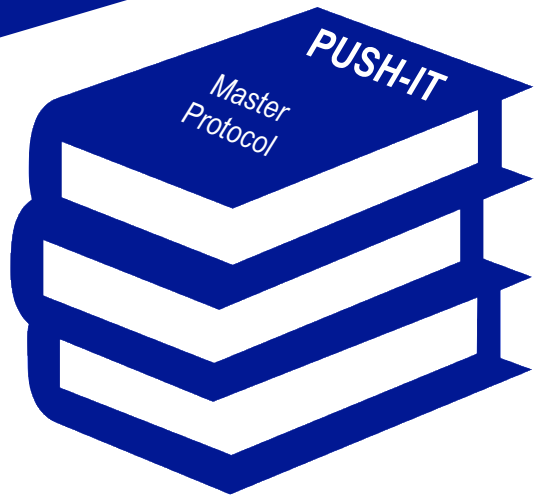


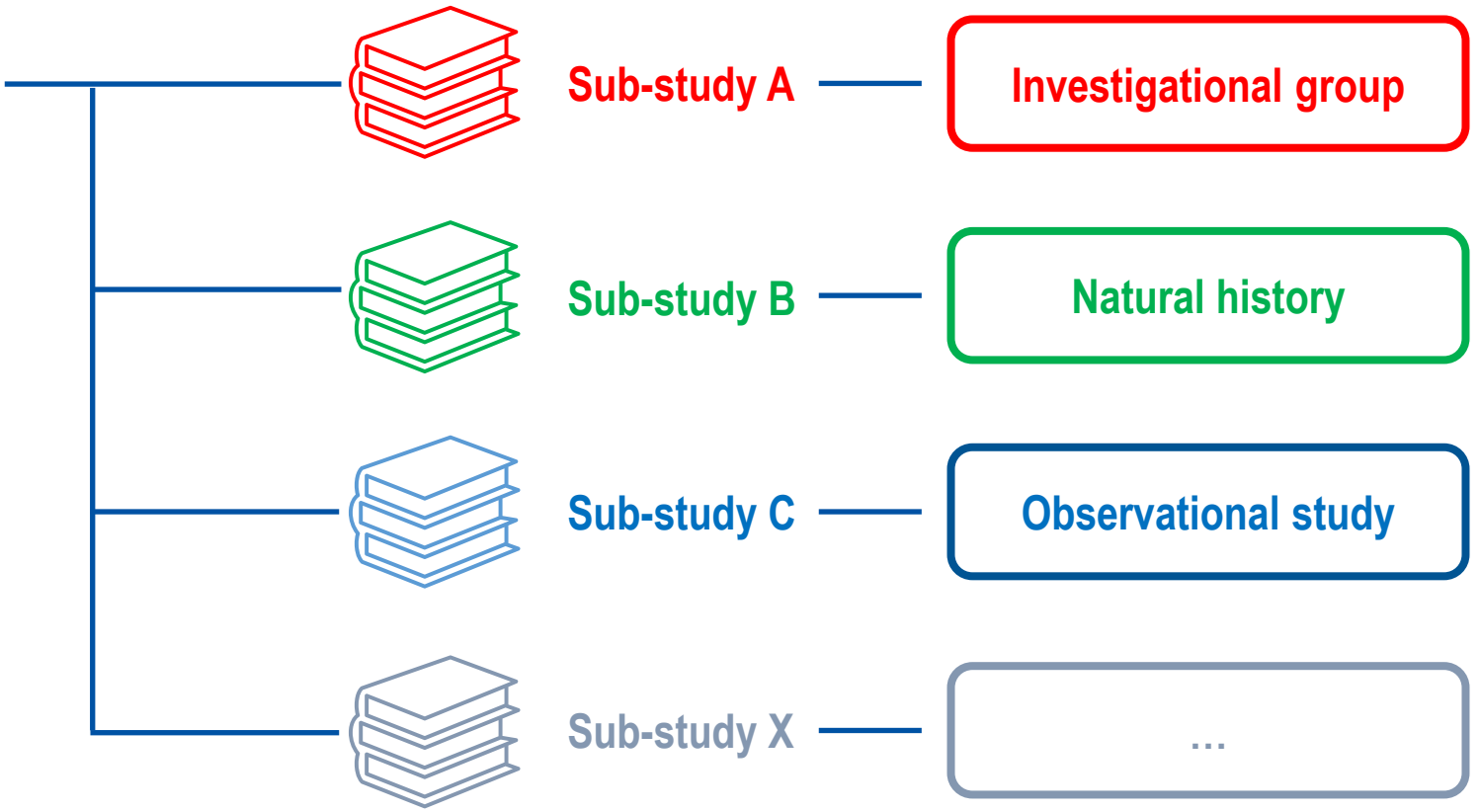


Investigational group

treatment A

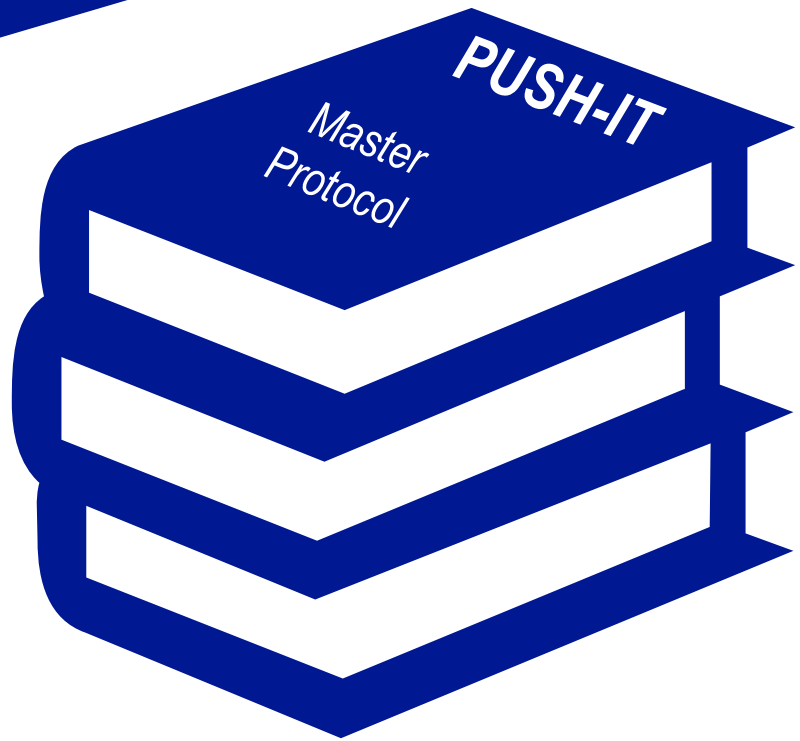
Single arm
options





Single arm

ORR in STS

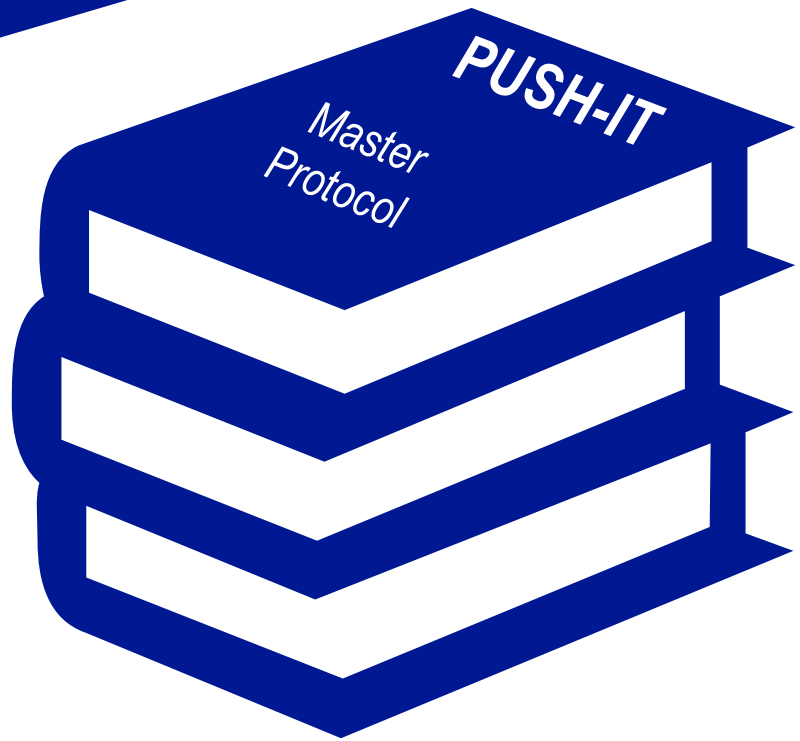


Investigational group — treatment A

Expected ORR will be on average “low”

→ **We need to exploit available data to improve our evaluation of drug activity**

External controls



Investigational group — Drug A

External control group — SoC

- = inclusion/exclusion criteria
- = radiologic assessments
- = items for clinical data collection

External controls

>50 Academic sites around the world

PUSH-IT Center

External controls

Experimental treatment

SoC

External controls

Experimental treatment

SoC

External controls

Experimental treatment

SoC

Observation only

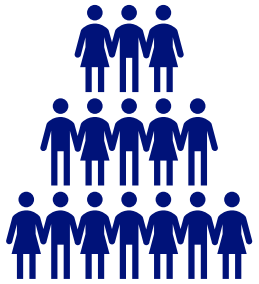
External controls

Genomic/Molecular data

- Individual patient data
- Pre/post treatment
- ctDNA
- Data sets

Previous trials

- Academic trials / IIT
- Cooperative groups
- Industry-sponsored
- PUSH-IT trials



Data from patients

- Patient Reported Outcome Measures
- APP-Based CRFs
- Registries from Patient Advocacy Groups

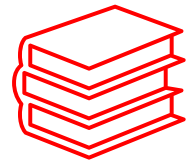
Academic Chart Reviews

- Comprehensive data extraction
- Institutional databases
- Registries

Real World Data

- Well-defined SoC
- Prospective off-label use of drugs
- Registries
- Repurposing effort

External controls



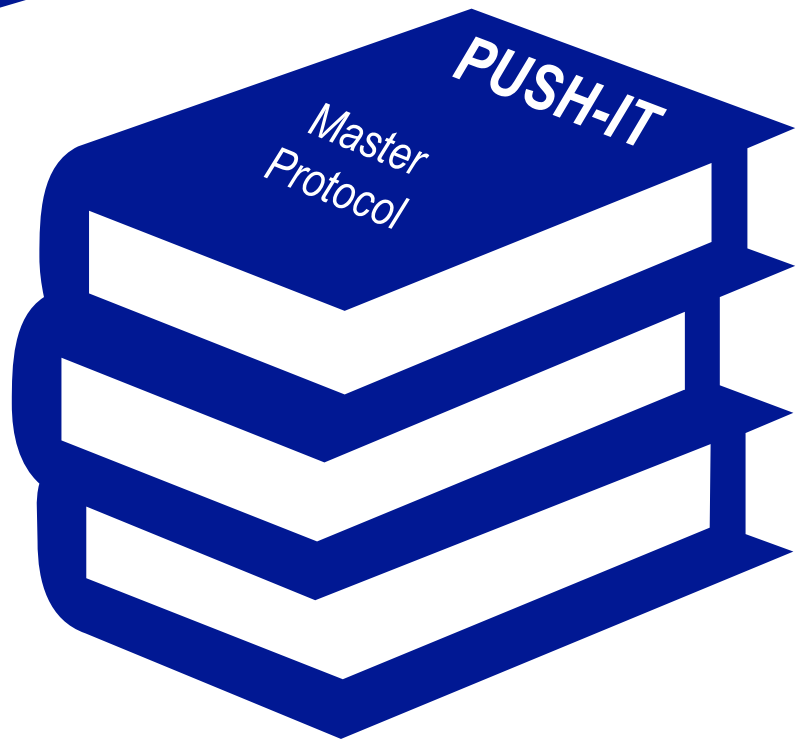
Investigational group — Drug A — Prospective, open-label phase 2 trial

External control group — SoC — Prospective observational trial in the same population Treated as per SoC (active surveillance, treatment, …)

- = inclusion/exclusion criteria
- = radiologic assessments
- = items for clinical data collection

Synthetic data?

Small RCT?



Investigational group — treatment A

R 1:1; 2:1; 4:1; bayesian; discontinuation; …

Standard/control group — SoC

Synthetic data?

Conclusions

- Work in progress
- Exploit PUSH potentials
- Maximize knowledge from each patient
- Looking for innovative approaches
- A starting point also for other rare tumors

PUSH PLATFORM

Question to EMA

Can we plan periodic meetings with

EMA (and FDA) to develop the PUSH-IT project?

Thanks!

Questions?

15’ coffee break

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

THE WORKSHOP WILL RE- START AT 15.15 PM CET 09.15 AM EST