

Ecraid studies overview

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UMC Utrecht, the Netherlands

VIG meeting
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ecraid



Where ECRAID comes from

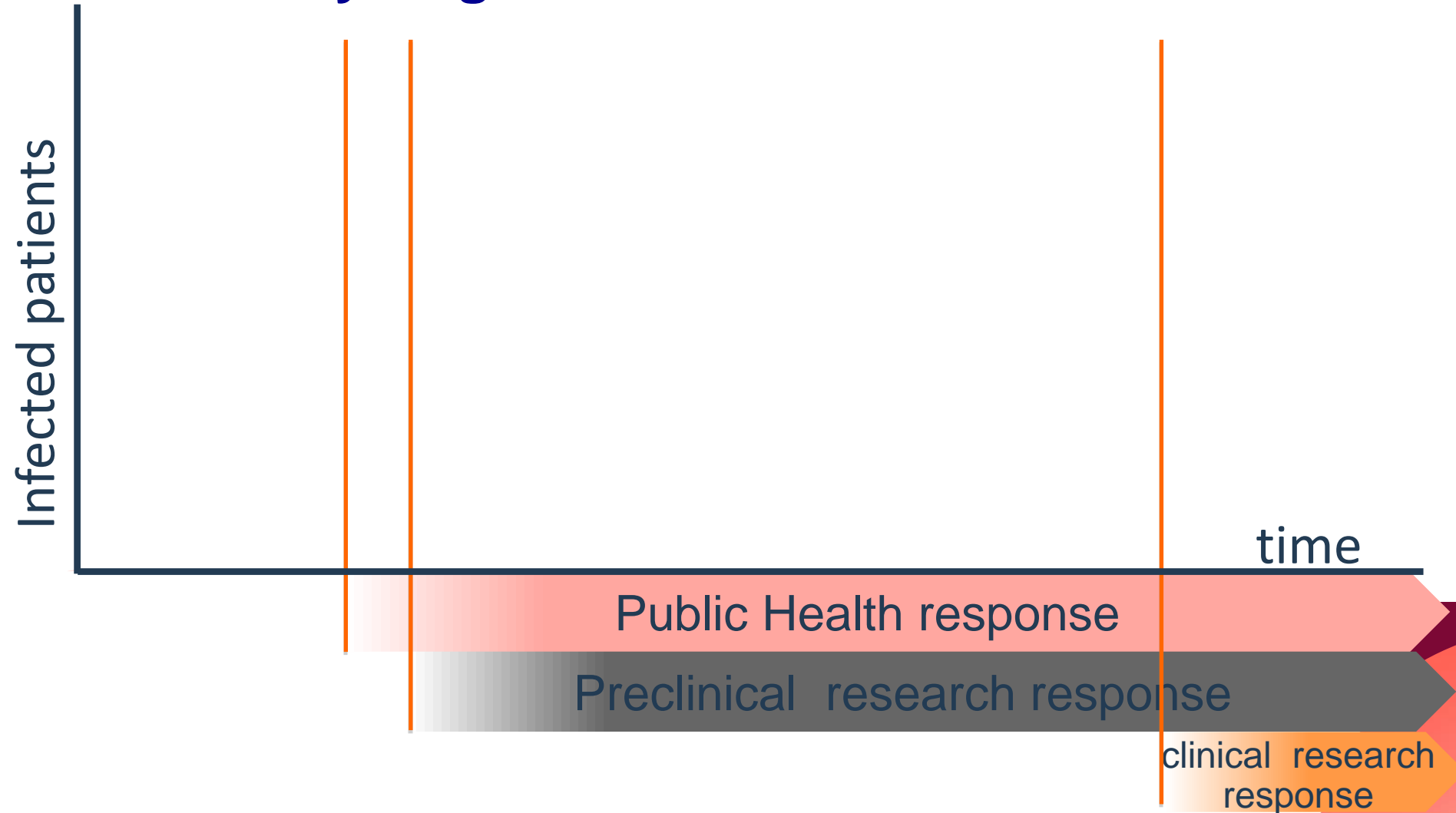
COMBACTE (IMI)

- **Aim: to enhance the efficiency of clinical evaluation of new antibacterial treatments**
- Create a self-sustaining premier antibacterial development network
- Expanding research and laboratory networks
- Optimal alignment of clinical trials with investigator sites
- Cutting edge molecular methodologies and trial design

PREPARE (FP-7)

- **Aim: To prepare a rapid scientific response to any severe infectious disease outbreak**
- Providing real-time evidence for clinical management of patients and for informing public health responses
- Cutting edge molecular methodologies and trial design
- Use the clinical trial network established in COMBACTE

Clinical research responses to ID outbreaks are usually fragmented and too late



PREPARE: fast-forward clinical research during epidemics to improve clinical management

Infected patients

time



Public Health response

clinical research response

Preclinical research response

COMBACTE 2014



2021



Hospitals

398



1086



Countries

36



42



Contacts

643



3.537



GCP trained

19



1025



Clinical studies

5



37



Patients enrolled

<100



39.552

1 Site performance indicators

A Quantitative – 1) enrolment rates, 2) contracting and ethical approval timelines, 3) contract timelines, 4) completion time eCRF, 5) response time to eCRF queries, 6) subject completion

B Qualitative – communication, infrastructure, challenges, successes, recommendations from study team

2

National
Coordinators Opinion

Site performance

3

Data from feasibility
questionnaires

4

Selected for an
interventional or
observational study

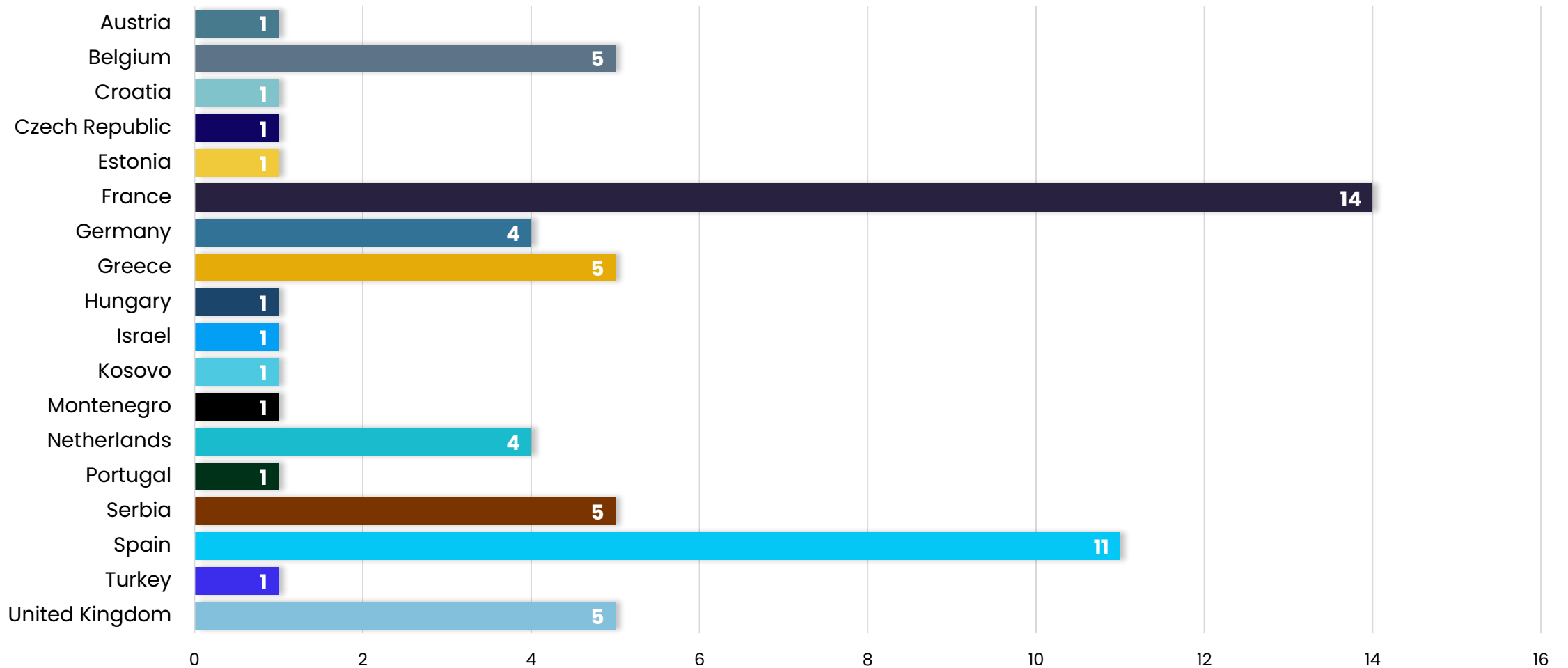
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Number of trials the
site is selected for

6

Country specifics

Country distribution – Top 50 Sites



Our goals

Operational excellence

- CLIN-Net and LAB-Net

Scientific innovation in trial design

- STAT-Net

Optimal sharing of epidemiological data

- EPI-Net

Optimal preparation for a scientific response

- PREPARE response modes

An example of executional excellence

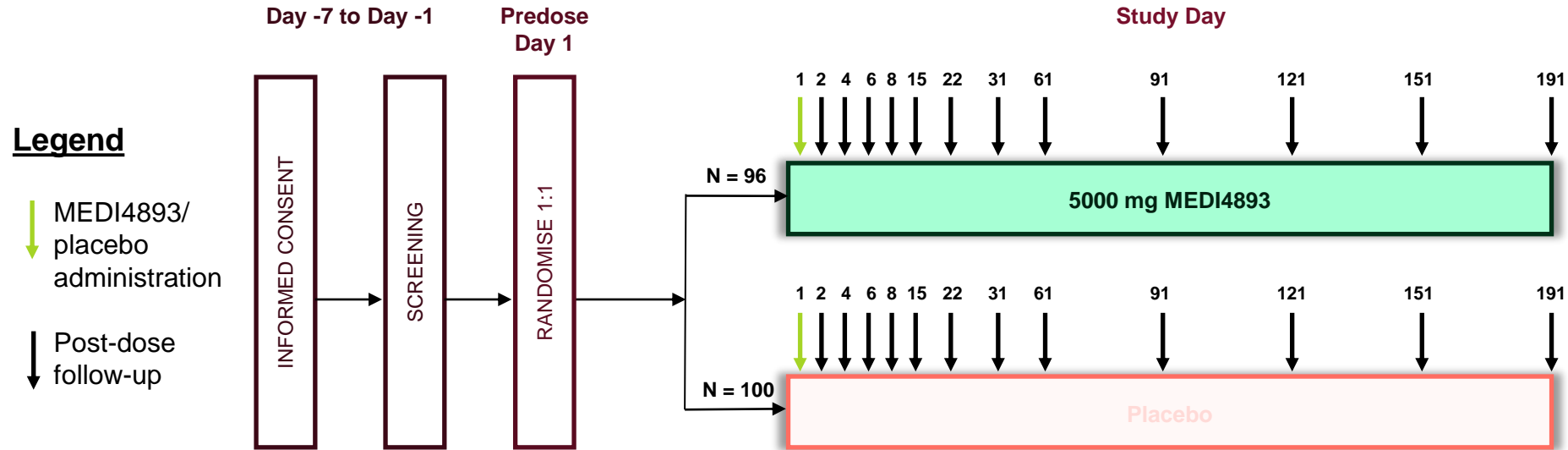
THE LANCET Infectious Diseases

Efficacy and safety of suvatamoxumab for prevention of *Staphylococcus aureus* ventilator-associated pneumonia (SAATELLITE): a multicentre, randomised, double-blind, placebo-controlled, parallel-group, phase 2 pilot trial



Bruno François*, Hasan S Jafri*, Jean Chastre, Miguel Sánchez-García, Philippe Eggimann, Pierre-François Dequin, Vincent Huberlant, Lucia Viña Soria, Thierry Boulain, Cédric Bretonnière, Jérôme Pugin, Josep Trenado, Ana Catalina Hernandez Padilla, Omar Ali, Kathryn Shoemaker, Pin Ren, Frank E Coenjaerts, Alexey Ruzin, Olivier Barraud, Leen Timmermont, Christine Lammens, Vadryn Pierre, Yuling Wu, Julie Vignaud, Susan Colbert, Terramika Bellamy, Mark T Esser, Filip Dubovsky, Marc J Bonten, Herman Goossens, Pierre-François Laterre, on behalf of COMBACTE Consortium and the SAATELLITE Study Group†

An example of executional excellence



- Critically ill patients without pneumonia, requiring prolonged ventilation were enrolled and tested by PCR to identify *S aureus* colonization in the lower respiratory tract
 - PCR: Fast (<2 hrs), easy to perform (<2 mins hands-on time)
 - PCR-positive subjects randomized to receive single IV infusion of either placebo or suvratoxumab
 - Followed closely for development of *S aureus* pneumonia (Primary Endpoint), adjudicated by an independent panel of blinded HAP/VAP experts and radio



Challenge: to have an incidence of 25% of the primary endpoint in the placebo group

An example of executional excellence

Efficacy against multiple pneumonia definitions in mITT population

Pneumonia Definition	Placebo N=100	Suvratoxumab N=96	RRR (90% CI) ^a	NNT ^b
S aureus Pneumonia ^c	26 (26.0%)	17 (17.7%)	31.9% (-7.5%,56.8%)	12
All Cause Pneumonia	30 (30.0%)	20 (20.8%)	30.6% (-4.9%,54.0%)	11
All Cause Pneumonia or Death	42 (42.0%)	31 (32.3%)	23.1% (-4.9%,43.6%)	10

Press Release: Aridis Pharmaceuticals Announces Exclusive License of suvratoxumab, a Phase 3-Ready Monoclonal Antibody, from AstraZeneca

Aridis Pharmaceuticals, Inc. (Nasdaq: ARDS) today announced that it has entered into an exclusive, worldwide licensing agreement with AstraZeneca (LSE/STO/Nasdaq: AZN) to in-license the late stage monoclonal antibody candidate, suvratoxumab.

"We intend to efficiently leverage our collaboration with the globally renowned HAP/VAP experts in the EU Commission's Innovative Medicines Initiative (IMI) **COMBACTE consortium** and our global network of existing clinical sites to launch the Phase 3 study for AR-320 in the 4th quarter this year," said Hasan Jafri, M.D., Aridis' Chief Medical Officer. "We are delighted that this Phase 3-ready candidate is supported by IMI through the **COMBACTE consortium** and are excited to demonstrate the potential for suvratoxumab to fulfill an unmet medical need in a highly vulnerable and high-risk population, while also offering substantial pharmacoeconomic benefits," said Dr. Jafri.

An example of executional non-excellence



29th **ECCMID** Amsterdam, Netherlands
13 – 16 April 2019

The congress of  ESCMID

L0011 Results of a Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Determine the Safety and Efficacy of a Single Dose of the Monoclonal Antibody Combination ASN100 for the Prevention of *Staphylococcus aureus* Pneumonia in Endotracheal Heavily Colonized, Mechanically Ventilated Subjects

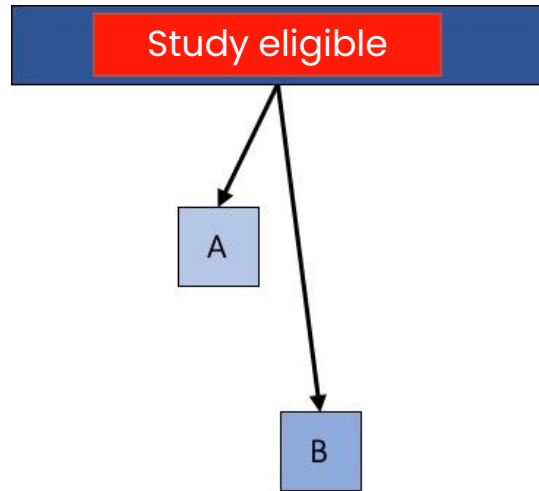
Zoltan Magyarics^{*1}, Karin Provost², Nimrod Adi³, Tomasz Czarnik⁴, Khatuna Japaridze⁵, Nikoloz Kartsivadze⁶, Mikhail Kirov⁷, Ed Campanaro⁸, Matthew Goodwin⁸, Lori Muir⁸, Marin Kollef⁹, Chris Stevens⁸

ASN100 is a combination of 2 fully human IgG1 mAbs, that together neutralize 6 *S. aureus* cytotoxins (alpha-hemolysin and 5 leukocidins)

The trial was terminated prematurely due to futility.

The incidence of *S. aureus* pneumonia (6%) was far below the expected rate (26%) based on previous reports, such that a reduction by ASN100 could not be adequately demonstrated in a study of this size.

An example of innovation in trial design



OPINION

NATURE REVIEWS | DRUG DISCOVERY

Adaptive platform trials: definition

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

ORIGINAL ARTICLE

This article was published on February 25,

ORIGINAL

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

AUGUST 26, 2021

VOL. 385 NO. 9

N Engl J Med 2021;385:777-89.

DOI: 10.1056/NEJMoa2103417

Therapeutic
in Noncritical

Therapeutic Anticoagulation with Heparin in Critically Ill
Patients with Covid-19

The ATTACC,

The REMAP-CAP, ACTIV-4a, and ATTACC Investigators*

Core to Ecraid is a European ‘warm-base’ clinical research network

300 primary care sites
in 18 European countries

1000 hospital sites
in 42 European countries

90 paediatric sites in 18
European countries

800 laboratories
in 41 European countries

ecraid

ORGANISED



The network has decision-making processes, common network policies, procedures, protocols and interoperable systems in place.

PREPARED



The network is prepared to rapidly initiate a clinical research response to emerging health threats in an agile and efficient manner.

ENGAGED



The sites are engaged in the network-level activities and decisions, with trusted relationships in place and contractual agreements negotiated.

RESOURCED



The sites are adequately resourced and staffed to efficiently perform high-quality clinical research studies.

ACTIVE



The sites are actively involved in recruiting patients in one or more Ecraid clinical studies, on a continuous basis.

TRAINED



The sites are well-trained in performing clinical and/or laboratory research activities, based on individual needs.

EXTENSIVE



The network has an extensive European geographic coverage, covering all clinical settings and infectious disease expertise.

SUSTAINABLE



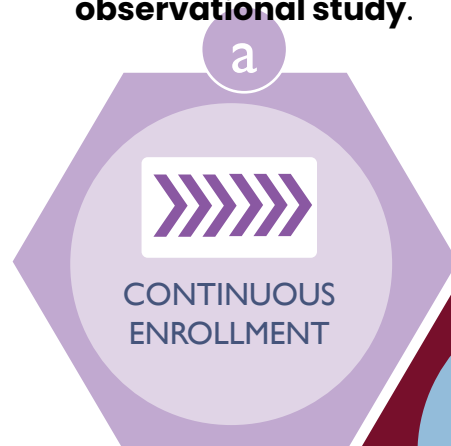
The network is financially sustainable, in support of its secure long-term continuity.

COVERING A WIDE RANGE OF CLINICAL RESEARCH

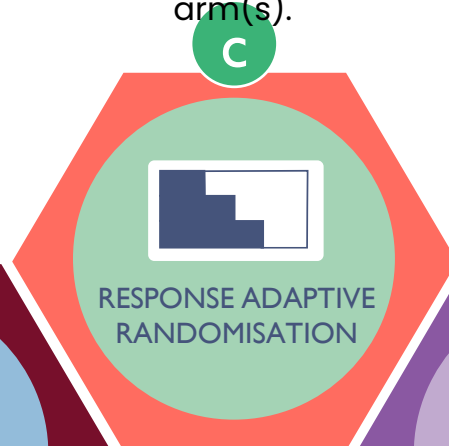
SPONSORS	› Investigator-initiated	Investigator-initiated (non-commercial) clinical studies on ID, addressing relevant clinical research gaps.
	› Industry-initiated	Industry-initiated (commercial) clinical studies on ID, supporting the development of commercial products or the gathering of market information.
TYPES OF STUDIES	› Observational	Studies aimed at the assessment of patients' epidemiological and clinical variables and patient treatment, gathering intelligence (data and/or samples) advancing our knowledge on specific ID indications, their clinical care and public health implications.
	› Interventional	Studies testing key aspects (e.g. safety, efficacy) of specific patient-level interventions, such as vaccines and therapeutics
TYPES OF RESEARCH	› Prevention	Clinical studies on preventive measures such as vaccines, infection prevention programmes or lifestyle changes and their impact on lowering risk of development or progression of disease.
	› Treatment	Clinical studies on treatments and treatment strategies such as therapeutic drugs, combination treatments and more complex treatment protocols.
	› Diagnostic	Clinical studies on diagnostics or medical devices and/or diagnostic approaches and their value for (early) diagnosis of disease(s) and/or causative pathogens and – where relevant – their antimicrobial susceptibility profile.
	› Screening	Clinical studies aimed at unravelling pathogenesis and biomarkers for severe outcomes.
	› Epidemiological	Clinical studies to gather epidemiological information on e.g., the incidence and spread of disease(s), characterisation of natural history of diseases and risk factors of disease to provide baseline for trials.
	› Quality of Life	Clinical studies aimed at exploring strategies to improve quality of life of patients with specific ID.
	› Health	Clinical studies aimed at testing the health-economic benefits of treatment, prevention, or diagnostic
TRIAL PHASES	› Phase I	First-in-human clinical studies in small groups.
	› Phase II	Evaluation of safety and efficacy of intervention in larger groups of individuals.
	› Phase III	Large clinical studies in patients evaluating an interventions effectiveness against current standards.
	› Phase IV	Post-approval studies to evaluate long term effects and potential further uses.

INNOVATIVE DESIGN ELEMENTS IN CLINICAL STUDIES

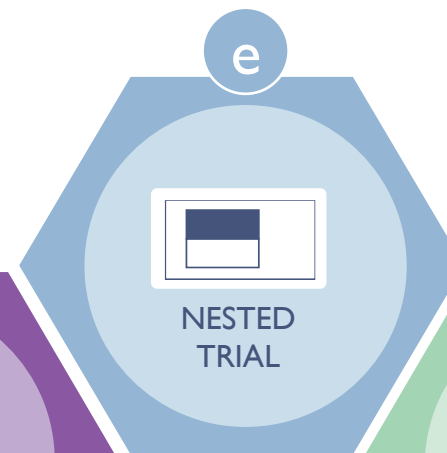
Continuous enrolment of patients, receiving standard-of-care for a defined disease indication, in a **perpetual observational study**.



Response Adaptive Randomisation, with intermediate analyses of trial results and intermediate preferential randomisation towards (the) better performing trial arm(s).



"Nesting" a clinical trial in an ongoing perpetual observational study, also known as "trial in cohort".



Two (or more) clinical trials **sharing a control group**.

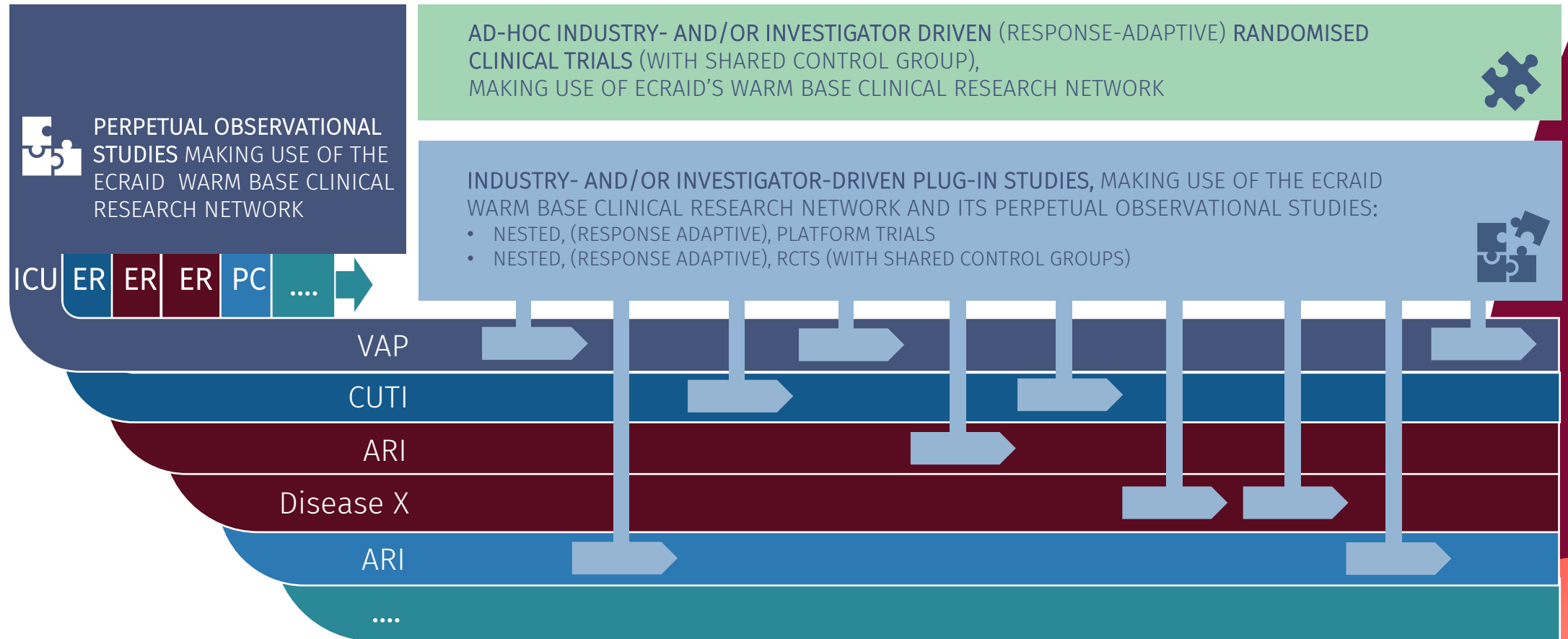


A master protocol which sets out trial procedures under one study design and across one trial infrastructure.



Clinical studies that are ongoing over time, with no pre-defined stopping time, with a **platform design** governed by a master protocol, that envisions adding and dropping trial arms.

TO BUILD A BROAD PORTFOLIO OF STUDIES



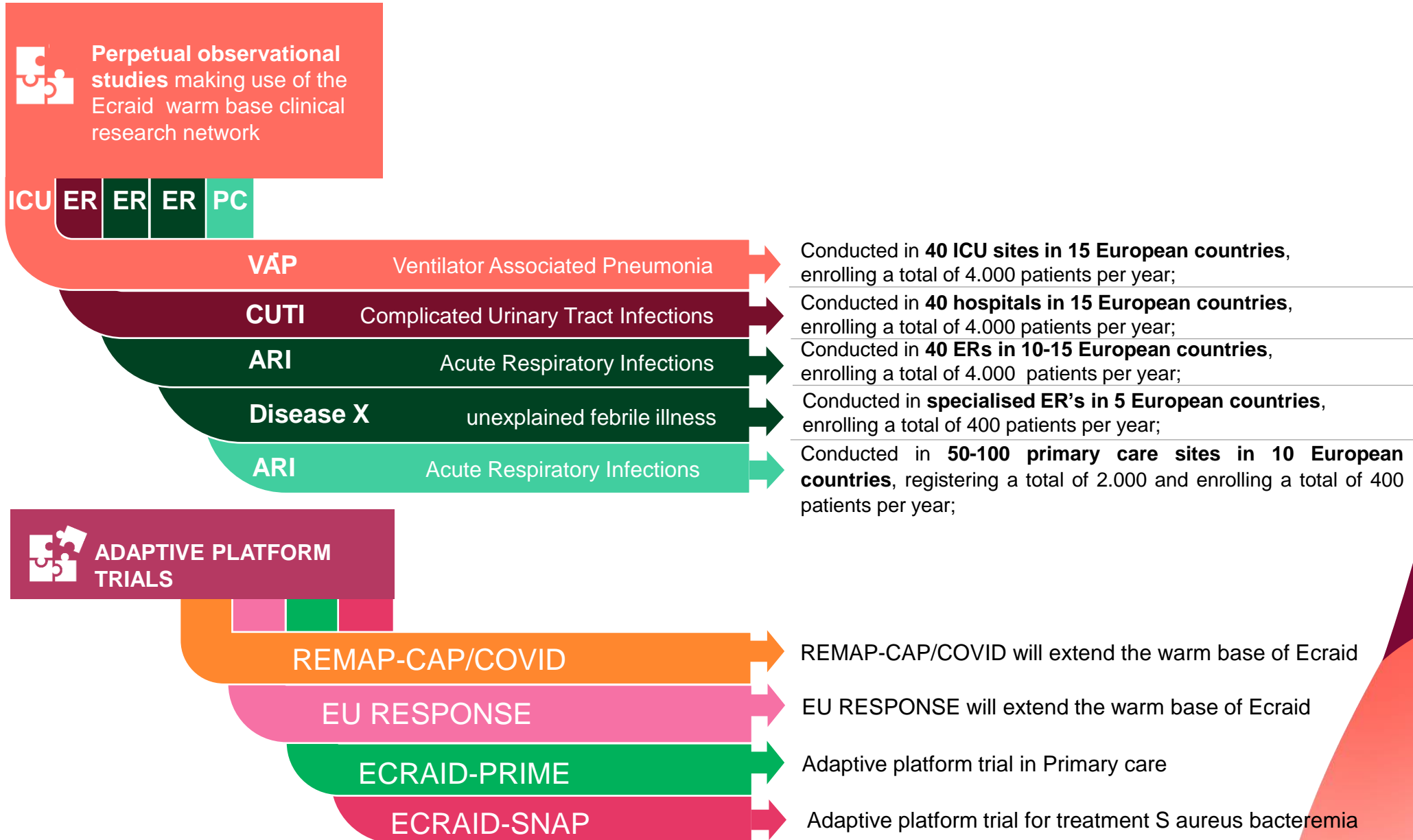
ICU = Intensive Care Unit
ER = Emergency Room
PC = Primary Care

VAP = Ventilator Associated Pneumonia
CUTI = Complicated Urinary tract Infections

ARI = Acute Respiratory Infections
ARBO = Arthropod-borne infectious diseases

➔ = individual plug-in study making use of the POS

Complemented with adaptive platform trials



How to be successfull

- Single-point of access for anyone interested in executing clinical trials
- Single sponsor (ecraid foundation for ecraid-driven studies)
- Master contracts with clinical sites & laboratories
- Streamlined study approval processes
- Pre-approved protocols for response activities
- Overarching data collection tool
- Professional dissemination of study findings and epidemiological data

Many thanks!

Visit us:

 www.ecraid.eu

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