COMBACTE

Combatting Bacterial Resistance In Europe

THE ISSUE

ANTIMICROBIAL RESISTANCE IN THE EU EVERY YEAR:

KILLS
25.000 People

COSTS THE ECONOMY
€ 1.5 Billion

CHALLENGES
In the development of new drugs

1. Scientific challenges
2. Regulatory challenges
3. Business challenges

ACTIONPLAN EUROPEAN COMMISSION
issued in 2011

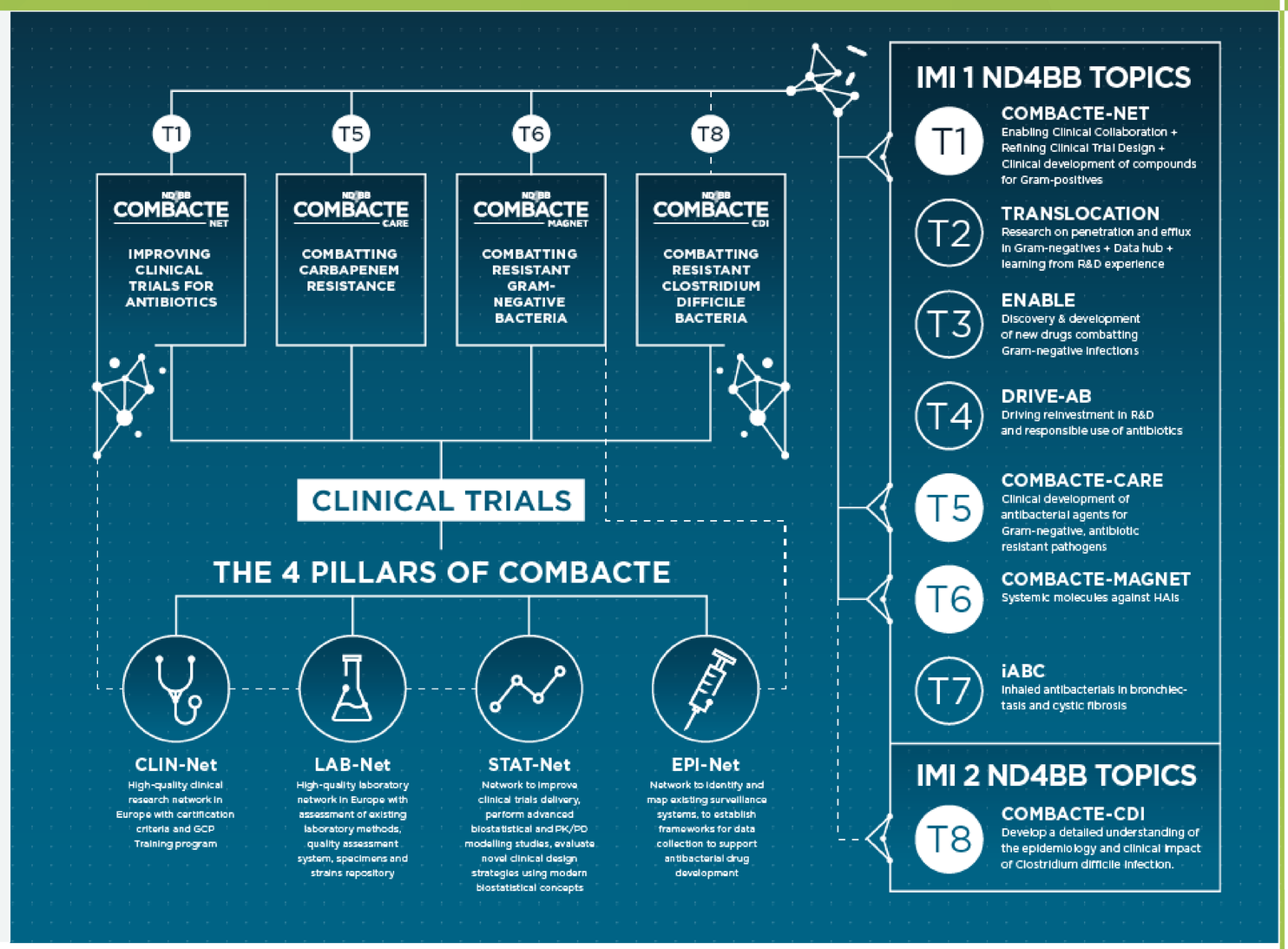
IMI NEW DRUGS 4 BAD BUGS PROGRAM
issued in 2012

UNIQUE COLLABO-RATION

IMI established an unprecedented partnership between industry, academia and biotech organizations to combat antibiotic resistance in Europe

OBJECTIVES

1. A self-sustaining antibacterial development network
   - ☑ Expanded research and laboratory networks
   - ☑ Optimal alignment of clinical trials with investigator sites
   - ☑ Clinical and epidemiological data
2. Increased efficiency of antimicrobial drug development
   - ☑ Align clinical trials with cutting edge molecular methodologies and trial design
   - ☑ Deliver clinical trials with various candidate compounds from MedImmune/AstraZeneca, Alcuris, Pfizer , Da Volterra, The Medicines Company



COMBACTE-NET

COMBACTE-NET aims to establish a high-quality, pan-European network of clinical sites, that will form the backbone for clinical studies within the wider ND4BB program.

CLINICAL TRIALS

Within COMBACTE-NET the following clinical trials are currently active:

SAATELLITE: A Phase II study to evaluate the effectiveness of Suvratoxumab (previously MEDI4893), a monoclonal antibody against alfa-toxin in *S. aureus*, in preventing *S. aureus* HAP/VAP in ICU patients. MEDI4893 was developed by AstraZeneca.
Status: Database lock has been achieved.

ASPIRE-ICU: A prospective, observational, epidemiologic cohort study of ICU patients with healthcare associated infections caused by *S. aureus* or *P. aeruginosa.*
Status: The 2.000 patient target has been achieved. The study is now in the process of site closing.

ASPIRE-SSI: A prospective, observational, epidemiologic cohort study of patients undergoing surgery to determine the incidence of *S.aureus* surgical site infections (SSI).
Status: 33 active sites enrolling patients. 8697 patients screened of which 3.750 have been enrolled in the study cohort. Target is 5.000 enrolled patients.

ANTICIPATE: a prospective observational cohort study of patients receiving antibiotic treatment during hospitalization to estimate: the incidence of *C. difficile* infections (CDI), antibiotic-associated diarrhea (AAD), and changes in the diversity and composition of the intestinal microbiota.
Status: 1007 evaluable patients enrolled. Currently Finalizing data analysis and manuscript writing.

ARTHR-IS: A retrospective multi-center study which aims to estimate the burden of *S. aureus* as primary cause of prosthesis infections (SA-PJI) after a hip or knee arthroplasty and their risk factors. Other objectives are to quantify the costs, number of hospitalizations, surgical procedures to treat and control the infection and finally the factors influencing therapeutic failure.
Status: Finalizing study protocol.

EXPECT: A prospective observational pilot study to investigate the feasibility and design of a Phase 3 clinical efficacy vaccine study. General practitioners in maximum 8 countries will recruit a total of 6,000 participants: adults aged 60-85 years with a history of urinary tract infections. Objective is to catch hospital admissions of invasive extraintestinal pathogenic E. coli (ExPEC) disease (IED) cases. The O-serotype distribution of ExPEC isolates from patients with IED will also be estimated.
Status: Finalizing study protocol.

COMBACTE-MAGNET

COMBACTE-MAGNET (Combatting Bacterial Resistance in Europe - Molecules against Gram-negative Infections) aims to improve our knowledge on biological markers of *P. aeruginosa* infections, transmission dynamics of these bacteria, and on the host-specific response to infections. Such knowledge will enable researchers to design more efficient and effective clinical trials of new molecules.

CLINICAL TRIALS

Within COMBACTE-MAGNET the following clinical trials are currently active or completed:

EVADE: To determine the efficacy of MEDI3902, a bispecific monoclonal antibody that inhibits two key virulence factors of *P. aeruginosa (*PcrV and Psl) in preventing *P. aeruginosa* HAP/VAP. MEDI3902 was developed by AstraZeneca, as a new way of preventing pulmonary *P. aeruginosa* infections without using antibiotics.
Status: 75 active sites enrolling patients. 785 subjects have been enrolled into the EVADE study of which 143 have been randomized.

RESCUING: a retrospective observational study to assess the clinical management and treatment outcomes of hospitalized patients with complicated urinary tract infections in countries with a high prevalence of multidrug-resistant Gram-negative bacteria, including Bulgaria, Greece, Hungary, Israel, Italy, Romania, Turkey, and Spain. Performed in collaboration with AiCuris.
Status: Completed. Published scientific paper.

AIC499: a new and potent member of the family of so-called beta-lactam antibiotics. Given alone or in combination with a beta-lactamase inhibiting drug (BLI), AIC499 has shown strong activity against a broad range of multidrug-resistant strains of *P. aeruginosa* and *Acinetobacter*, both in laboratory and animal studies. AIC499 is being developed by AiCuris.

COMBACTE-CARE

COMBACTE-CARE (Combatting Bacterial Resistance in Europe-Carbapenem Resistance) aims to improve our knowledge on clinical management and outcomes of hospitalized patients with Carbapenem Resistant *Enterobacteriaceae* (CRE) infections; to analyse clinical and microbiological data to provide new insights for novel clinical trial designs; and to make recommendations
for the development of novel antibiotics to treat resistant infections.

CLINICAL TRIALS

Within COMBACTE-CARE the following clinical trials are currently active:

EURECA: a prospective observational study to assess the clinical management of patients with infections caused by CRE or carbapenem-resistant *Acinetobacter*. It will be supported by an already operational cohort for the identification of biomarkers in critically ill patients.
Status: Patient recruitment completed with 2266 patients enrolled.

REJUVENATE: a Phase IIa trial to evaluate the pharmacokinetics and safety of the combinational drug Aztreonam-Avibactam (ATM-AVI) in patients with complicated intra-abdominal infections. ATM-AVI is being developed by Pfizer.
Status: Final clinical study report delivered.

REVISIT: a global, phase III clinical trial designed to evaluate the safety, efficacy and tolerability of ATM-AVI for the treatment of serious infections due to Gram-negative bacteria including metallo-β-lactamase (MBL) producing MDR pathogens.
It is also supported by the US Government's Biomedical Advanced Research and Development Authority (BARDA) via a portfolio agreement with Pfizer.
Status: Up to 170 sites will be selected, of which up to 80 will be in the COMBACTE region.

COMBACTE-CDI

Clostridium difficile infection (CDI) is one of the most prevalent infections associated with health care, affecting both hospitalized patients and individuals in the community. Notably, there is an increasing realization that cases may also occur in people not recently exposed to antibiotics or other health care interventions. CDI carries a considerable level of threat, with far-reaching impacts in both endemic and epidemic settings. It is a major cause of diarrhea and more serious intestinal conditions, such as colitis. Infections pose an extensive burden in terms of morbidity, mortality and health care resource utilization, so they require effective prevention and management strategies

WP1: A large epidemiology study to quantify the burden of *C. difficile* infections – in terms of incidence , distribution , recurrence , morbidity and transmission – across the healthcare economy.
Status: 119 sites recruited from 12 countries. Sample collection completed, case/control study launched.

WP2: Assess current practices in Europe and their potential impacts, including guidelines, testing, surveillance, treatments and costs.
Status: survey launched.

CONTACT INFORMATION

Visit us at booth 1.84 in the exhibition hall!
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ND4BB COMBACTE

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