STRIVE

ACTIV INSIGHT018

Strategies and Treatments for Respiratory Infections and Viral Emergencies

Experience with launch of global treatment trials during the pandemic

EMA Lessons Learned workshop, 9th June 2023

Prof Jens Lundgren, University of Copenhagen
Chair, INSIGHT & STRIVE scientific steering committees, global PI for STRIVE

STRIVE ACTIV INSIGHT018

insight

INSIGHT – global ID trial network

- Launched in 1990's – initial focus on HIV RCT's
  - ESPRIT [1] (n=4,111), SMART [2] (n=5472), START [3] (n=4,684) (FU completed in end of 2021)
    - 30-40% participants from Europe
- After 2009 Influenza pandemic
  - Passive immunity trial, published in 2019[4]
- During COVID pandemic
  - ACTT, ACTIV-3 and now STRIVE (next slides) + ITAC[5] and OTAC

- Funding from US NIH, ANRS, MRC, Australia, Germany, Denmark
- EU legal sponsor: CHIP, Univ of Copenhagen
- Compliant with GDPR regulations

[1] NEJM 2009; [2] NEJM 2006, Ann Intern Med, 2008;
[3] NEJM 2015, NEJM Evidence 2023;
[4] Lancet Respir Med 2019; [5] Lancet 2022

ACTT - Remdesvir

- Protocol finalized mid February 2020
- Europe – via INSIGHT – involved 1st March
- FPI in Europe (DK, Germany, Spain, Greece; UK):
  - 26th March (15% of total n=1,025)
  - Last patient randomized on 27th April
- Extraordinary pace of regulatory approval process
- Seamless establishment of contractual and legal framework *within* network – regionally and globally – relied on long-term relationships
  - US NIH had CTA with relevant pharma company (arm-length principle)

Beigel *et al*, NEJM 2020

ACTIV-3 TICO

- April 2020: ACTIV="Accelerating COVID-19 Therapeutic Interventions and Vaccine" - an NIH led public-private partnership - started 6 platform trials focusing on out and in hospital studies
- ACTIV-3/TICO – Network of Networks[1] led by INSIGHT- formed June 2020
  - Platform RCT – 6 studies [2] (phase 2-3) – hospitalized patients
  - Master protocol and first study ready by 1st Aug 2020
    - FPI : 5 Aug; FPI in Europe (DK, Germany, Spain, Greece, UK): mid Sep 2020 – 17% of total n=2,625
  - Regulatory evaluation: regulators had diverse understanding of usefulness of platform trials during a pandemic (also within EU; several EU countries were unsuccessfully engaged). EU agreed to "English text" labels. Expiry date !

[1] INSIGHT, PETAL, CTSN, VA

[2] NEJM 2020, Ann Intern Med, 2021, 2022 Lancet ID, 2022 & Lancet Resp Med 2022, 2023

STRIVE

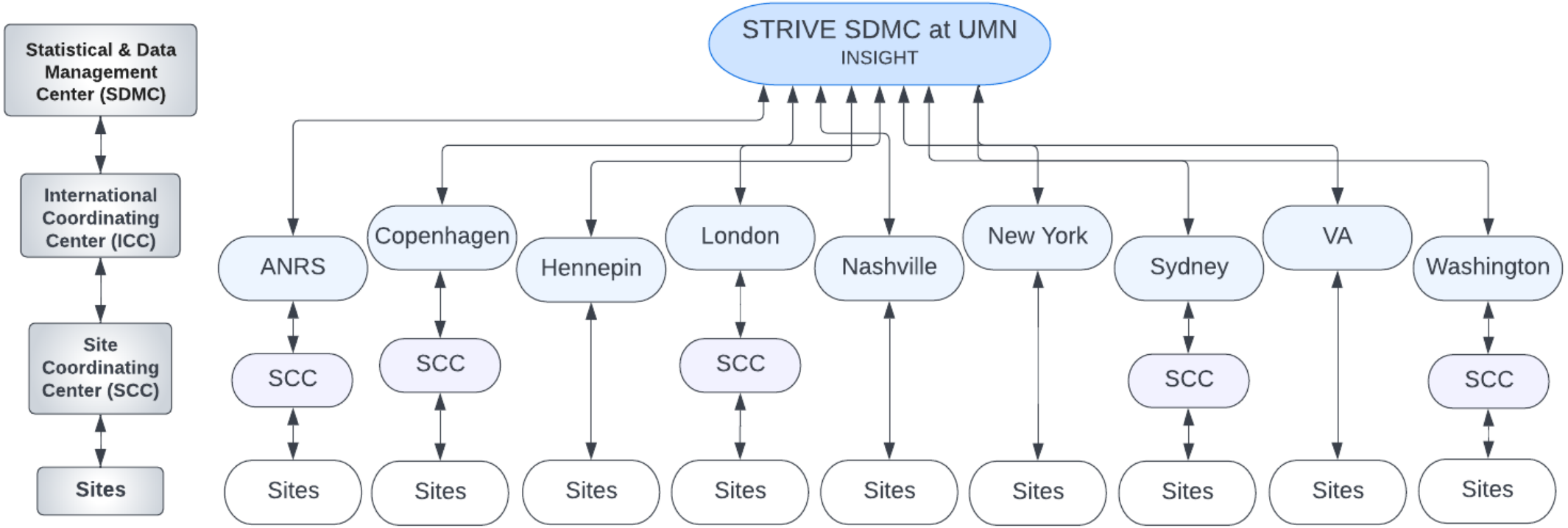
- Launched in April 2022 – joining US ACTIV platforms (ACTIV 1, 3, 5) into one single network, aiming for a suitable global research platform as part of pandemic preparedness – led by INSIGHT
- Purpose:
  - Identify better treatments for severe respiratory infections
  - Maintain agile clinical trials infrastructure for pandemic preparedness & rapid response
- Patient population: patients hospitalized due to acute respiratory infection
- Scope:
  - COVID-19 – initial focus
  - Influenza
  - Other known respiratory pathogens
  - Emerging pathogens
- 250+ clinical sites

STRIVE ACTIV INSIGHT018

insight

STRIVE Consortium Infrastructrue

250+ sites in 35+ countries across 6 continents coordinated via
9 International Coordinating Centres (ICC's) feeding data to one central database



Central database

Oversee SCC's and sites

Oversee sites

Unidirectional communication & delegation of responsibility

Regulatory Evaluation of STRIVE

- Globally, regulatory agility slowed markedly vs early in pandemic
  - Discord: primary endpoint, intensity of safety data collection for phase 2-3 studies.
  - FDA discussion to resolve took 7 months
  - After master protocol approval – can review of new studies within be accelerated?
- CTIS experience:
  - Helpful to have one platform for both regulatory and ethics evaluation
  - Label of study medicine – only "English label"
    - Booklet labels are time-consuming (3-6 months)
  - QP release when importing to EU – potential major slow down factor
  - Requires expertise as not intuitive and is time consuming (1 FTE)
    - January 2023: submitted
    - Primo February: validated (kinks had to be sorted)
    - March: fair comments/critiques received and responded to
      - As response time is 12 days – large team required to be prepared to work full-time
    - Primo May – decision:
      - Approved: DK, Spain, Germany, Greece
      - Rejected: Poland (based on issues raised and accepted by other member states)

STRIVE and agility

- Motto: “catching the waves”
  - Trials needs to be done during epidemic surges
  - Surges not synchronized across the global
  - Experienced trial research infrastructure
  - Clinical trials addressing clear unmet needs
- Requires rapid
  - Protocol development
  - Regulatory approval
  - Distribution of study medicine and other trial-related “hard-ware”
  - Rapid activation of ALL sites able to enroll during surges

1. Complex and interlinked processes involving multiple stakeholders across 35 countries.
2. The more trials done via the consortium the quicker these steps are accomplished

Summary

- An established trial network (INSIGHT), with global reach, was able to rapidly engage during the pandemic
  - Regulatory process in EU
    - Initially very rapid review time; process slowed down
    - EMA (Health Threats and Vaccines Strategy group) facilitated verbal dialogue
    - CTIS assisted in coordinating views across EU member state regulators
- STRIVE continues to optimize agile launch and execution of trials
  - Optimize toward: FPI within 14 days of protocol completion and all sites globally open for enrolment within 100 days
  - Require revisions of contingency plans involving all stakeholders (regulatory, legal (clinical trials agreement, contracts) and scientific (protocol language))
  - A hard felt plea: regulators globally coordinate opinions on trials conducted via STRIVE (and other global pandemic trial platforms)

Acknowledgements

- *STRIVE leadership:* Jim Neaton, Ab Babiker, Jason Baker, Vicky Davey, Annetine Gelijns, Ginny Kan, Jens Lundgren, Gail Matthew, Wes Self, Bill Powderly, David Vock, Mike Kurilla & Cliff Lane
- *STRIVE science committee*
- *UoM:* Cavan Reilly, David Vock, Nicole Engen, Birgit Grund, Shweta Sharma, Eileen Dennings, Tom Murray, Greg Grandits
- Staff at STRIVE 9 ICC's, Site Coordinating Centres and site investigators – too many to mention, but an absolutely great and collaborative team
- Biospecimen shipment and analysis: Katy Saliba, Robin Dewar, Weizhong Chang, Brad Sherman, Norman Gerry (ABML) & Biorepository evaluation committee
- DCR @ NIAID: Cliff Lane, Laura McNay, Libby Higgs, J Tierney, Adam Schechner, *et al*
- Foundation NIH: Stacey Adam *et al*
- Funders: NIAID, ANRS, Australian, UK, Danish Governments
- Companies: Shionogi, BMS
- **Participants**