Tan Tock Seng HOSPITAL

Framework of Singapore ID Clinical Research Network (SCRN)

Ding Ying

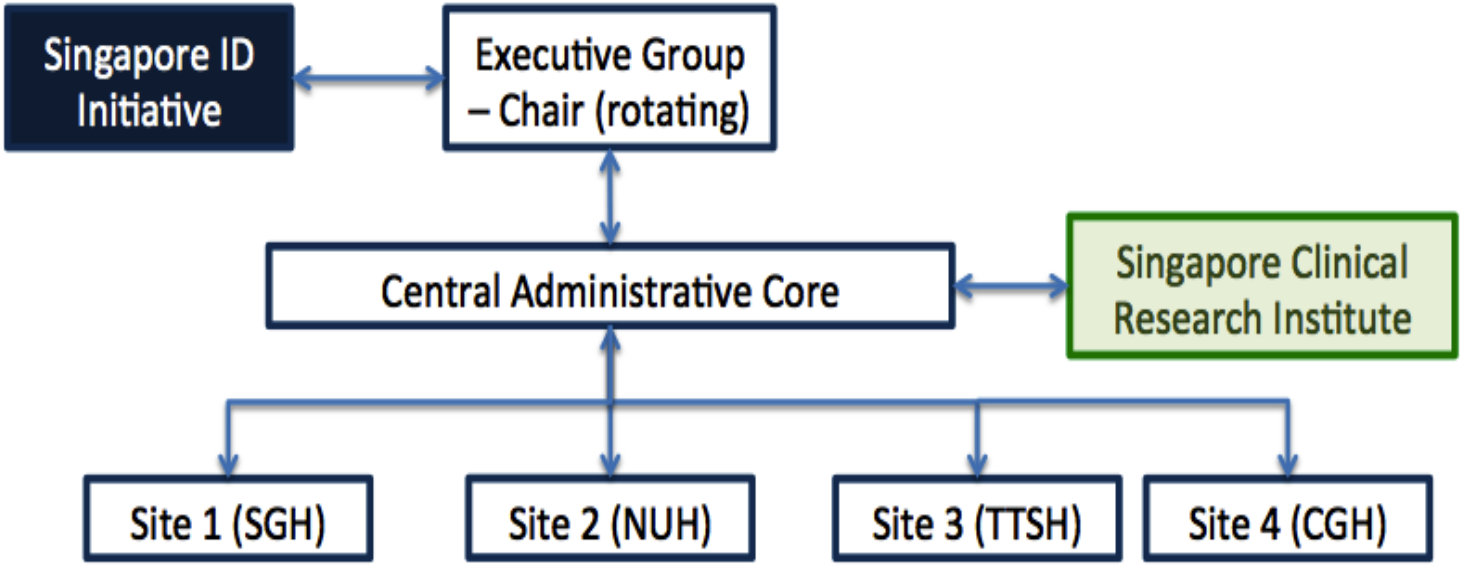
May 2014

Background

- Crossed-institutional projects in Infectious disease and clinical microbiology are becoming more common and important globally.
- Clinical research networks have been successfully established in US, UK, and Australia&NZ.
- In Singapore:
  - ID clinical research projects confined to laboratory-based and basic science projects. Cross-institutional clinical trials are rare
  - Each hospital will not have enough patient-subjects to conduct a full clinical research
  - Heavy workload of ID clinicians and clinical microbiologists
  - Lack of infrastrucutural support for sustained clinical research
  - ID physician and clinical microbiologists have little tranning and experience in clinical research. Particularly in the conduct of clinical trial

Singapore ID Clinical Research Network

- Funded by SIDI, Based at IIDE, TTSH.
- PI : Prof Leo Yee Sin



Singapore ID Clinical Research Network

- **Goals:**
  - Establish long-term research collaboration between clinical infectious diseases (and related) departments in Singapore.
  - Perform clinically relevant and practice-oriented research on local infectious diseases.
  - Incorporate a culture of research in ID and clinical microbiology practice in Singapore.

Singapore ID Clinical Research Network

- **Roles:**
  - Assist with implementation of individual projects:
    - Protocol development assistance
    - Prepare and submit clinical research-related documentation.
    - Assist with administrative issues across all participating sites
    - Provide manpower assistance (i.e. RA's)
  - Establish the initial network
  - Eventually become a mature clinical research support unit
  - Function as immediately available capacity for clinical research in the event of an outbreak

Singapore ID Clinical Research Network (SCRN)

PI: Prof Leo Yee Sin

Co-investigators

Admin Manager: Soh Siew Hwa
Network Coordinator: Ding Ying
Senior Research Fellow: Ng Ee Ling

Research Assistants:

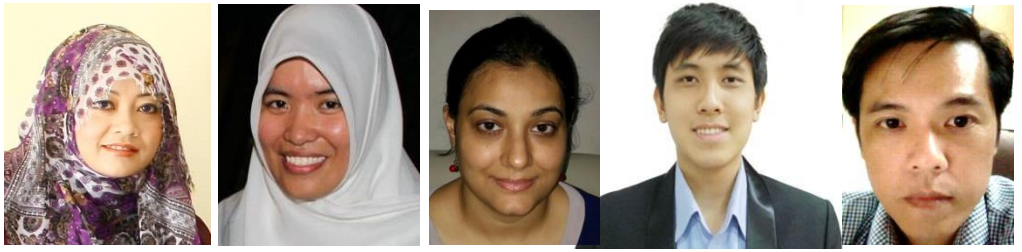
TTSH: Norhudah Bte Othman

SGH: Siti Maryam Abdul Rahman

NUH: Shilpa MUKHERJEE

Floater RA: Wong Wei Jie

Calvin



Projects facilitated by SCRN

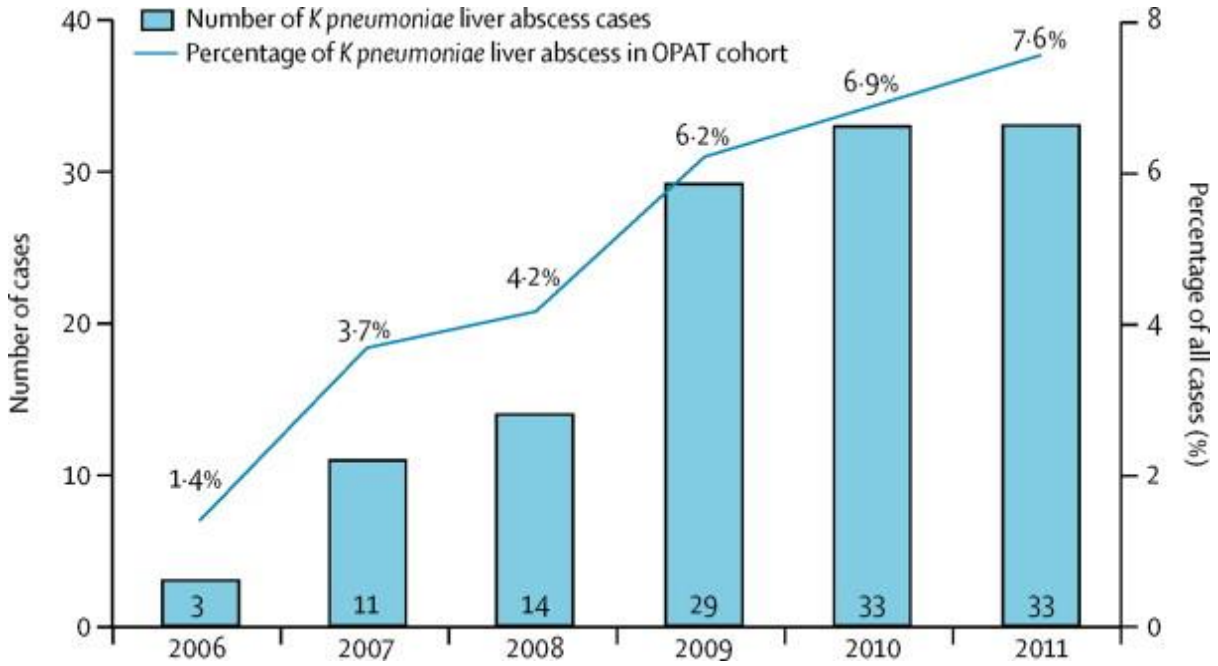
- Multi-centers, Multi-national
- 7 clinical studies, 5 RCTs
- 1 PK/PK study
- 1 prospective observational study

S/N	Project Title	PI	Collaborating Institutes	Funding Agency	Duration
1	**An open-label prospective randomised controlled non-inferiority trial comparing oral to intravenous antibiotics in the early management of Klebsiella liver abscess (A-KLASS)**	Dr. Sophia Archuleta, (NUH)	NUHS, SGH, TTSH	NMRC and SIDI	3 years

A-KLASS-Background

Klebsiella Liver Abscess:

- Most common cause of liver abscess in Singapore (70%)
- Associated with diabetes, which is increasing significant burden on inpatient & OPAT departments
- No evidence or guidelines to guide total duration of antibiotics, or when to step down to oral antibiotics



Seetoh T, Lye D, Archuleta S, Fisher D. Lancet Infect Dis. 2013 May;13(5):391-2.

A-KLASS

Aims & Hypothesis

Primary Aim

- This study aims to compare the rate of clinical cure (measured at 12 weeks) with 4 weeks of intravenous antibiotics compared to early step-down to oral antibiotics in patients with KLA.

Secondary Aims

- To compare the total cost of each intervention
- To compare subject Quality of Life in each arm
- To investigate host and pathogen factors influencing susceptibility to *Klebsiella pneumoniae* infection and prognosis

Hypothesis

- Intervention (early step-down to oral antibiotics) is no greater than 12% inferior to our active control (continued intravenous antibiotics)

AKLASS: Total Recruitment Summary

	NUH	TTSH	SGH	TOTAL
Recruitment Start Date	5-Nov-13	9-Dec-13	27-Jan-14	-
Total Prescreened	184	142	108	434
Total Liver abscess cases	33	38	22	93
Total Eligible	22	25	8	55
Total Declined	9	14	3	26
a. by patient&family	5	13	3	21
b. by primary team	1	1	0	2
c. by investigators	3	0	0	3
Total Missed	1	0	0	1
Monitoring	0	0	0	0
Withdrawal	0	1	0	1
Total Recruitment	12	11	5	28
a. Oral Arm	6	5	3	14
b. IV Arm	6	6	2	14
Recruitment Rate	54.5%	44.0%	62.5%	50.9%
Total Target	52	70	30	152

* Reporting period till 15th May 2014

Projects facilitated by SCRN (cont'd)

S/N	Project Title	PI	Collaborating Institutes	Funding Agency	Duration
2	**Multicenter Phase IIB open-label randomized controlled trial on the efficacy of combination antibiotic therapy for serious infections caused by extensively drug-resistant Gram-negative bacteria (XDR-GNB)**	Dr. David Lye (TTSH)	SGH, CGH, NUHS	SIDI	2 years
3	**Population pharmacokinetics and pharmacodynamics of Polymyxin B and optimal dosing regimen in the treatment of extensively drug resistant gram negative bacterial infections (XDR PD/PK study)**	Dr. Lawrence Lee Soon-U (NUHS)	SGH, CGH, NUHS, TTSH	CDPHRG	3 years

Projects facilitated by SCRN (cont'd)

S/N	Project Title	PI	Collaborating Institutes	Total amount awarded	Duration
4	**A multi-centre open label randomized controlled phase IIB trial comparing Vancomycin versus Daptomycin for the treatment of Methicillin Resistant Staphylococcus aureus bacteremia due to isolates with high vancomycin minimum inhibitory concentrations (MRSA)**	Dr. Shirin Kalimuddin (SGH)	SGH, NUH, TTSH	SIDI	2 years
5	**Carbapenemase producing Enterobacteriaceae in Singapore (CaPES)**	Dr. Kalisvar Marimuthu (TTSH)	CGH, NUHS, SGH, TTSH, KTPH, Parkway	SIDI	2 years

CaPES: Total Recruitment Summary

	NUH	TTSH	JGH/AH	KTPH	SGH	CGH	Private	TOTAL
	13-Jan-14	13-Jan-14	-	22-Jan-14	09-Dec-13	-	-	-
Total screened/ eligible	15	21	-	-	144	-	-	180
Total rejected	1	2	-	-	33	-	-	36
Total missed	2 Passed away: 1 Discharged: 1	8 Passed away: 1 Discharged: 7	-	-	64 Passed away: 18 Discharged: 46	-	-	74
Total monitoring	3	1	-	-	7	-	-	11
Total recruited	9	10	-	-	40	-	-	59
% recruited	60.0%	47.4%	-	-	27.8%	-	-	32.8%

* Reporting period till 15th May 2014

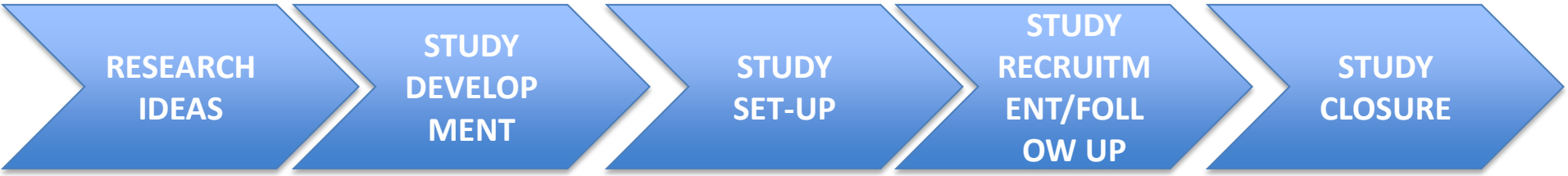
Projects facilitated by SCRN (cont'd)

S/N	Project Title	PI	Collaborating Institutes	Total amount awarded	Duration
6	**Controlling Antimicrobial use through Reducing unnecessary treatment of Catheter associated Urinary Tract Infections. (CARCUTI)**	Prof Paul Anantharajah Tambyah, NUHS	NUH, TTSH, SGH	CDPHRG	3 years
7	**Randomised Controlled Trial of meropenem versus piperacillin-tazobactam for definitive treatment of bloodstream infections due to third generation cephalosporin non-susceptible Escherichia coli and Klebsiella spp. (MERINO)**	Dr David Iye	NUH, TTSH, Australia, NZ		6 month

Current Issues and Challenges

- Ethics issues
- RA training Programme
- Strategies to increase recruitment Rate

Future Prospective



- Study design/proposal development
- Sample size estimation, randomization scheme, blinding procedure, and sampling scheme
- Planning statistical analysis approach
- Collaboration on grant applications for research projects.
- Site selection

- Protocol preparation and implementation
- Study budget preparation,
- Preparation of essential study documentation
- Ethics submission and CTC application
- Site personnel training
- Oversight for protocol compliance, adherence to Good Clinical Practice and Standard Operating Procedures,
- Study progress reporting,
- Management of timelines, budget and deliverables.
- Study investigator product management

- Statistical support
- Data analysis
- Manuscript publication

Thank You!

Email:
ying_ding@ttsh.com.sg