



# The effect of TB treatment on QuantiFERON-TB Gold In-Tube® responses

CBE Chee<sup>1</sup>, KW KhinMar<sup>1</sup>, SH Gan<sup>1</sup>, TMS Barkham<sup>2</sup>, CK Koh<sup>1</sup>, S  
Liang<sup>3</sup>, YT Wang<sup>1</sup>

<sup>1</sup>TB Control Unit, Tan Tock Seng Hospital, Singapore

<sup>2</sup>Dept of Microbiology, Tan Tock Seng Hospital, Singapore

<sup>3</sup>Yong Loo Lin School of Medicine, National University of Singapore

***2<sup>nd</sup> Global Symposium on IGRAs, Dubrovnik, Croatia  
30.5.09.***

# Background

- There is a need for new biomarkers for monitoring TB treatment
- It is hypothesized that quantitative T-cell responses to *Mycobacterium tuberculosis*-specific antigens reflect antigen burden and therefore disease activity
- Several longitudinal studies with ELISpot method showed declines in SFCs with active TB treatment
- Two studies with QFT reported declines with active TB treatment <sup>1,2</sup>; one study showed no decline <sup>3</sup>

<sup>1</sup> Kobashi et al. *Clin Infect Dis* 2006;43:1540-1546

<sup>2</sup> Katiyar et al. *Int J Tuberc Lung Dis* 2008;12(10):1146-1152

<sup>3</sup> Pai M et al. *Infection* 2007;35(2):98-103

AIM : To evaluate the effect of TB treatment on qualitative and quantitative QuantiFERON-TB Gold In-Tube<sup>®</sup> (QFT-IT) responses

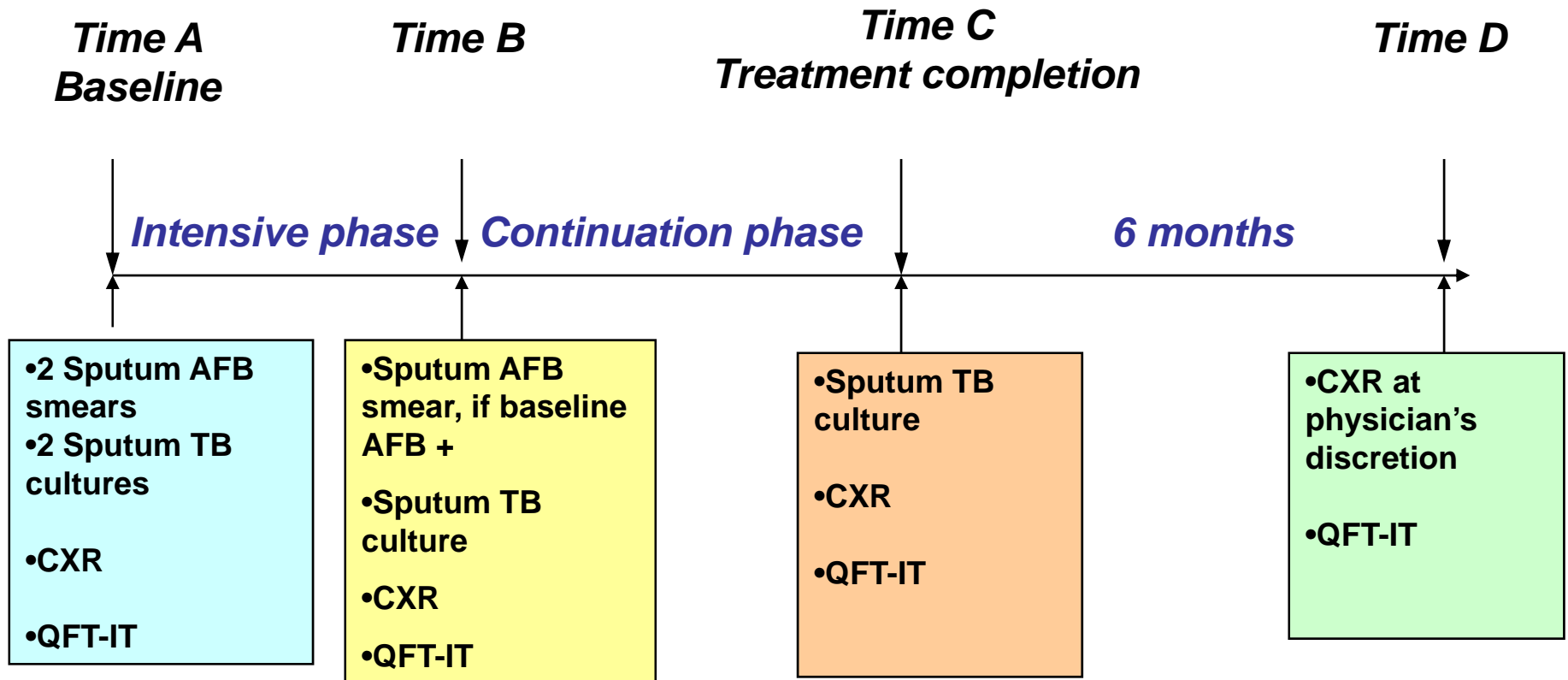
- Setting : Singapore TB Control Unit (TBCU), the national referral centre where ~60% of country's cases are treated
- Patients : Adult and adolescent patients treated for pulmonary TB (pTB) under programme conditions



# Methods

- Pulmonary TB patients who were sputum AFB smear-positive or clinically and radiologically deemed likely to be sputum culture-positive were enrolled within two weeks of starting treatment
- Excluded patients
  - with poor prognosis (eg. frail elderly, those with concomitant advanced malignancy)
  - who could not be followed for relapse (eg. those not residing permanently in Singapore)

# Methods



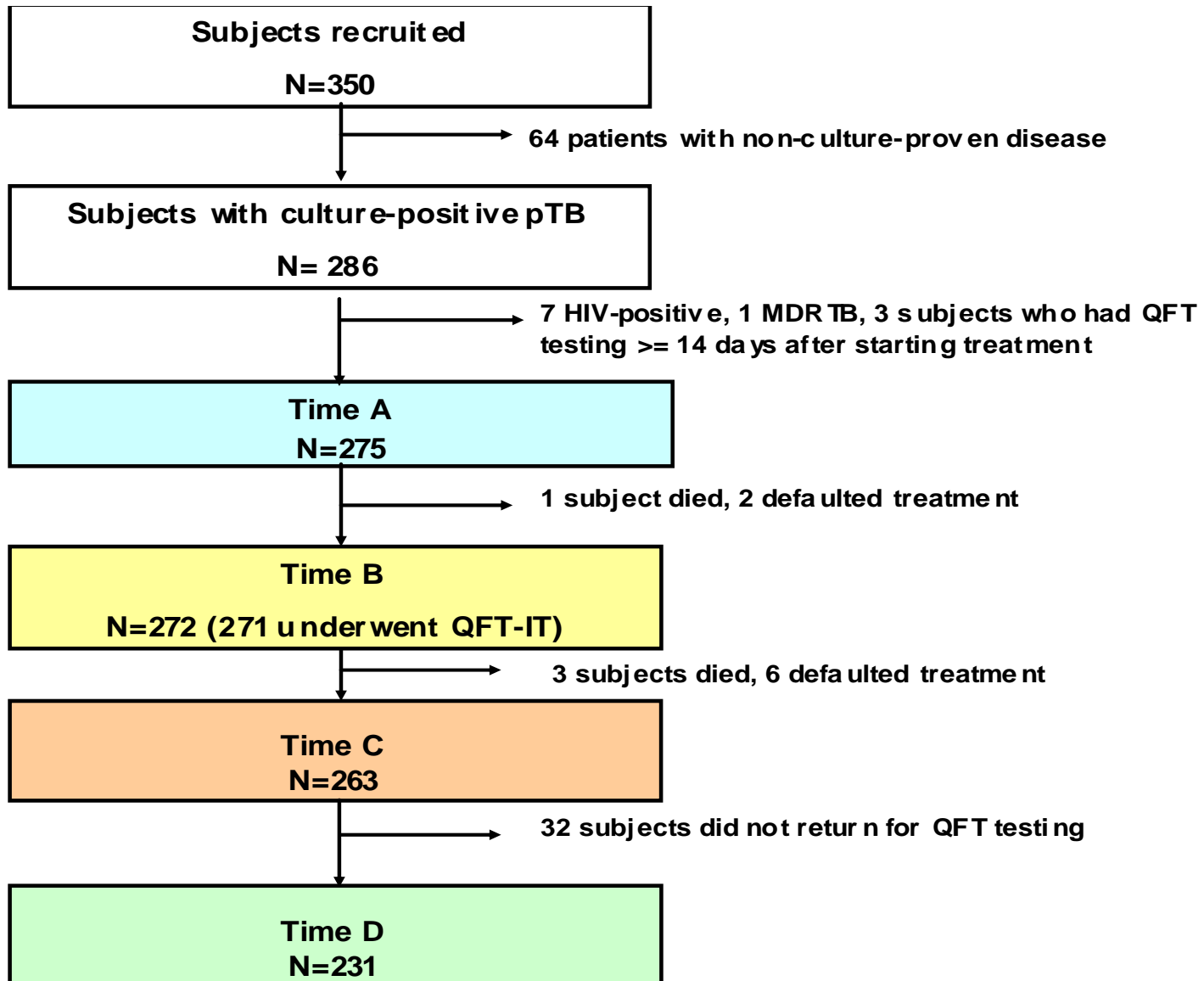
All patients routinely offered HIV testing

Baseline random blood glucose and liver enzymes routinely performed

# Methods

- Patients underwent TB treatment according to centre's protocol
  - Standard Short-course Chemotherapy under DOT at their nearest outpatient public health clinic
    - Patients with risk factors for hepatotoxicity were started on 9-month, non-PZA containing regimen
  - Physicians blinded to IGRA result
- QFT-IT
  - Performed according to manufacturer's instructions at TTSH Microbiology Lab
- Statistical Analysis performed using SAS 9.1
  - Generalized estimated equation (GEE) model for binary outcome using logit link used for analyzing qualitative QFT results
  - Mixed model was used for analyzing quantitative QFT results

# Study flow-chart

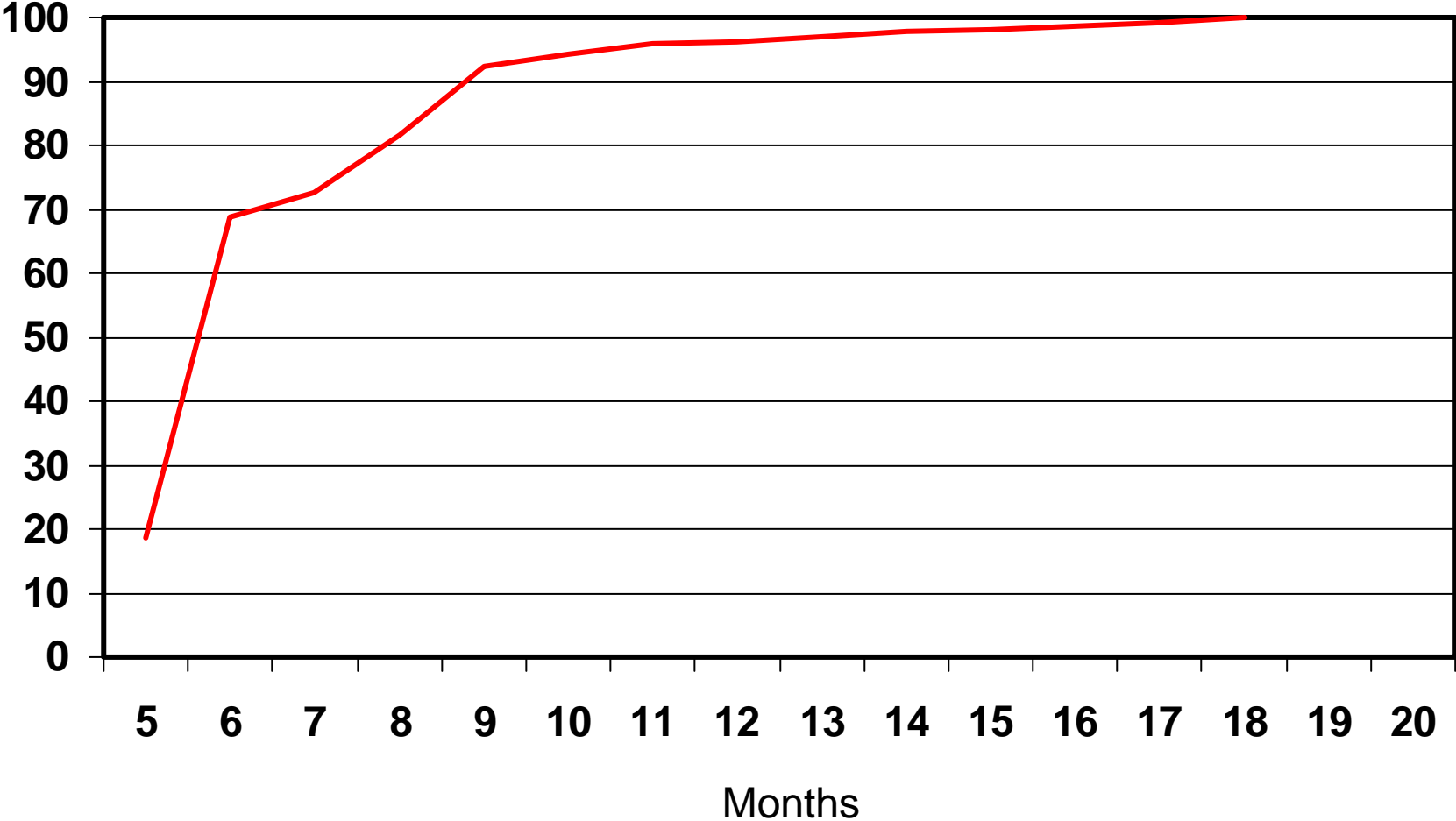


# Baseline Patient Characteristics (n=275)

Characteristic	Number (%)
Mean Age (range)	47.2 years (16.5 - 76.7)
Male	203 (73.8)
<u>Ethnicity</u>	
Chinese	186 (67.6)
Malay	65 (23.6)
Indian	14 (5.1)
Others	10 (3.6)
Diabetic	99 (36.0)
Mean BMI (range)	20.1 (12.0 – 34.5)
Current or ever-smoker	153 (55.6)
Sputum smear positive	210 (76.4)
Presence of cavity on initial chest radiograph	140 (50.9)

# Time to treatment completion (N=263)

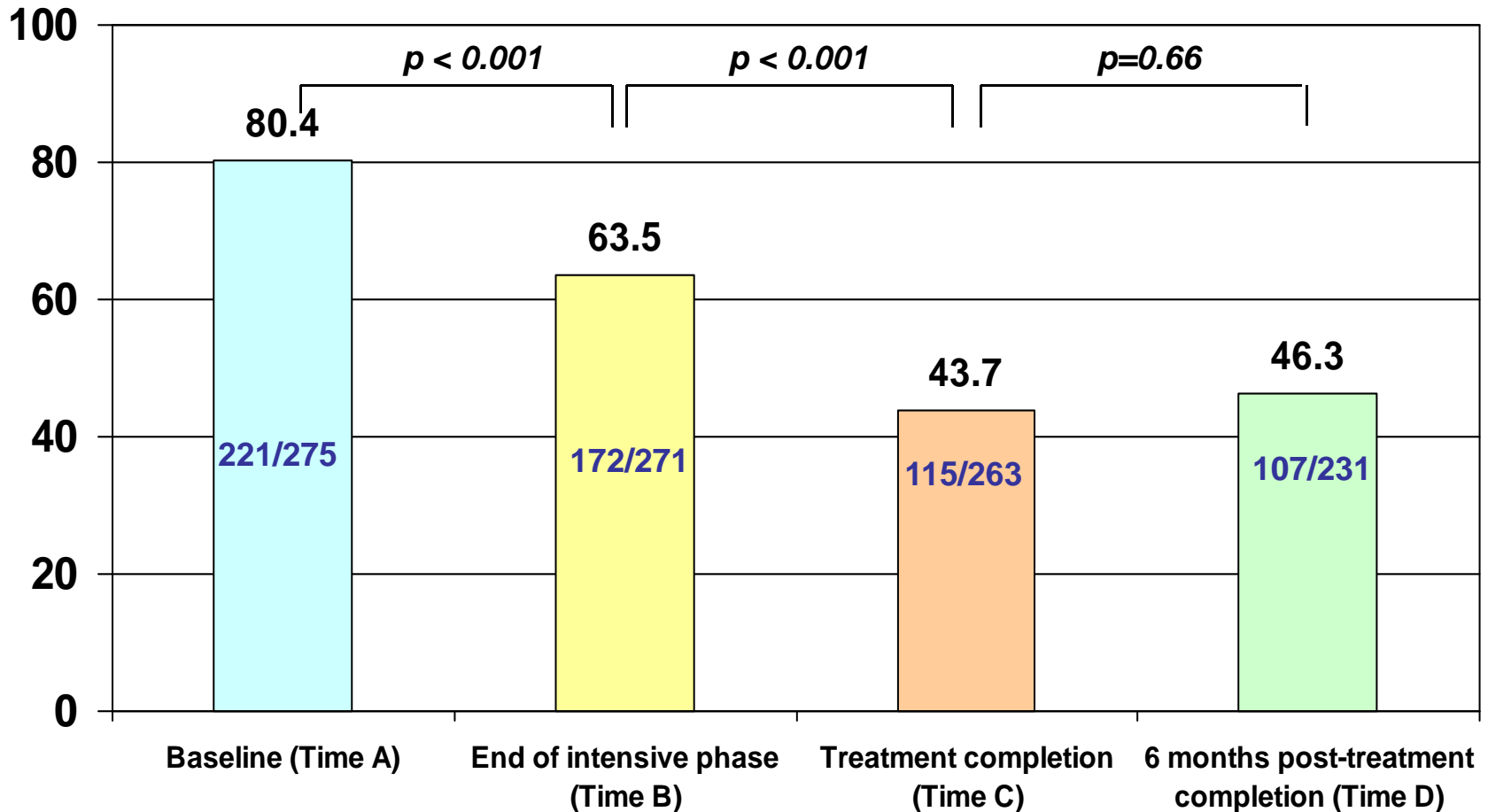
% of patients



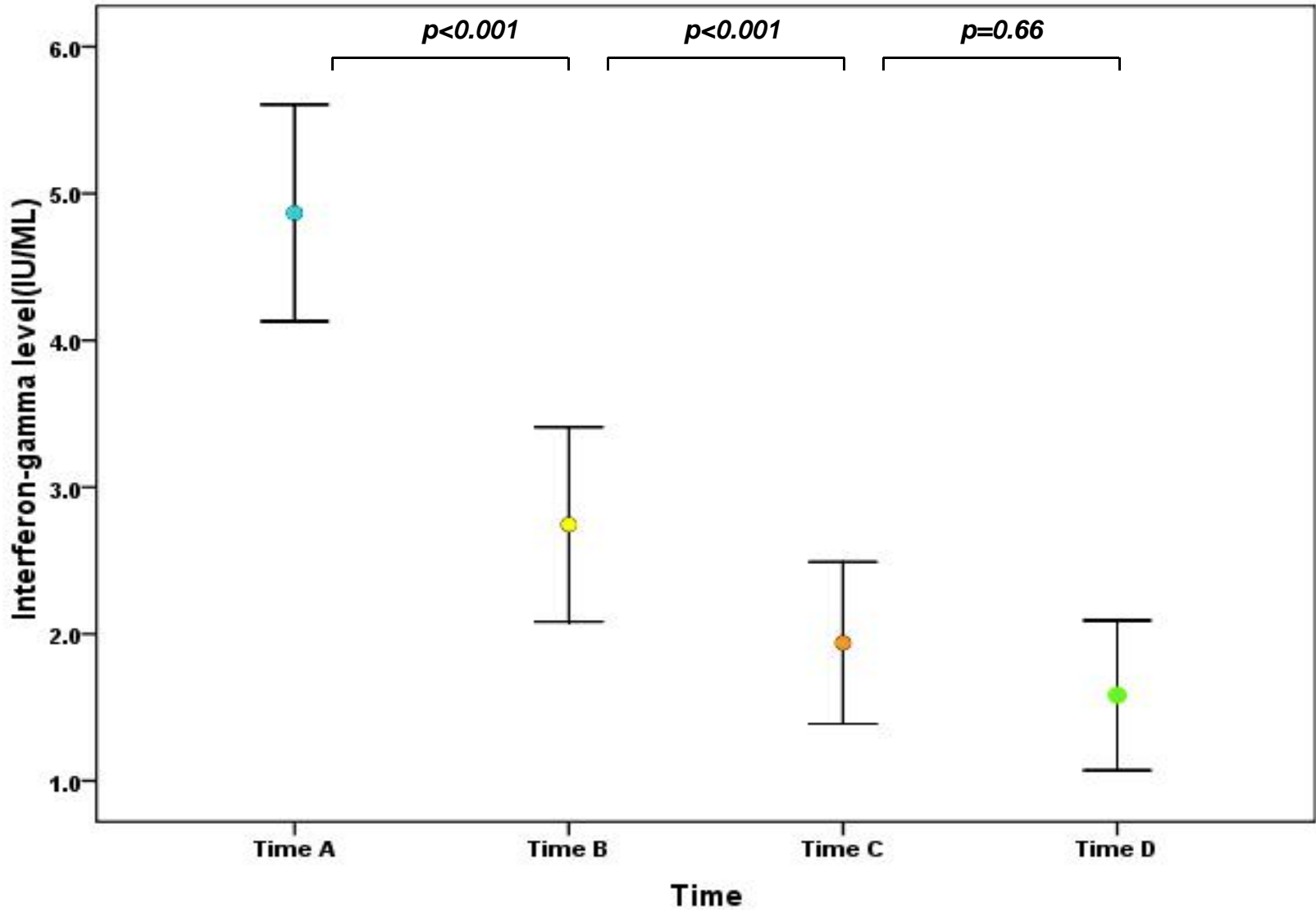
# QFT-IT results

- Total of 1040 samples
- No. of indeterminate results = 23 (2.2%)
- Indeterminate results considered as “non-positive” results in analysis

# Percent positivity of QFT-IT at each treatment time-point



## Quantitative titres (mean with CI) of QFT-IT at each treatment time point



# Summary

- This study showed significant declines in qualitative and quantitative QFT-IT responses with TB treatment
- There was no further decline in the qualitative or quantitative results from treatment completion to 6 months thereafter
- 44% and 47% were QFT-IT positive at treatment completion and 6 months post-treatment completion respectively

# Conclusion

- Serial tracking of quantitative QFT-IT responses may potentially be useful for monitoring TB treatment progress
- Isolated positive responses cannot be used as indicators of disease activity; these responses cannot be used as diagnostic aids in previously treated pTB patients

*Thank you*

**Acknowledgments**

Agampodi Pereira, Ee Xuan Yau, Kwee Yin Han, and all staff of  
Control Clinic

**Funded by National Medical Research Council grant  
1004/2005, Ministry of Health, Singapore**