Gynecologic Cancer InterGroup
Cervix Cancer Research Network

THE OUTBACK TRIAL

A Phase III trial of adjuvant chemotherapy following chemo-radiation as primary treatment for locally advanced cervical cancer compared to chemo-radiation alone

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Cervix Cancer Education Symposium, January 2019, South Africa

Treatment of locally advanced disease

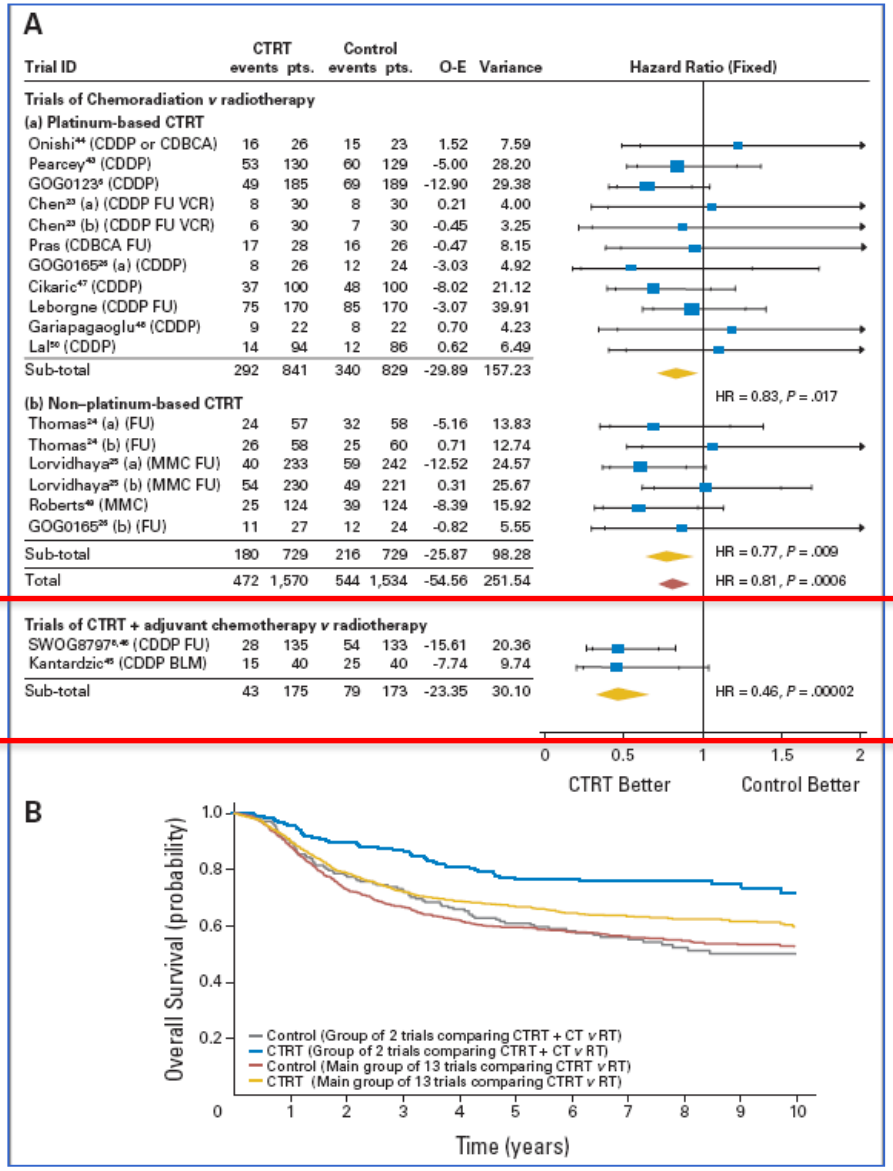
- Concurrent cisplatin and radiation the standard of care for locally advanced disease for FIGO stage 1B or higher: NCI alert in 1999

- Individual patient data meta-analysis of 18 trials confirmed benefit of concurrent chemo:
  - significant improvement in 5 year OS rate: (60 to 66%)
  - significant improvement in 5 year DFS rate (50 to 58%)

- Most deaths due to development of distant metastatic disease: CAN WE DO BETTER?

Chemoradiotherapy for cervical cancer meta-analysis collaboration: JCO 2008

How can we reduce distant failures?

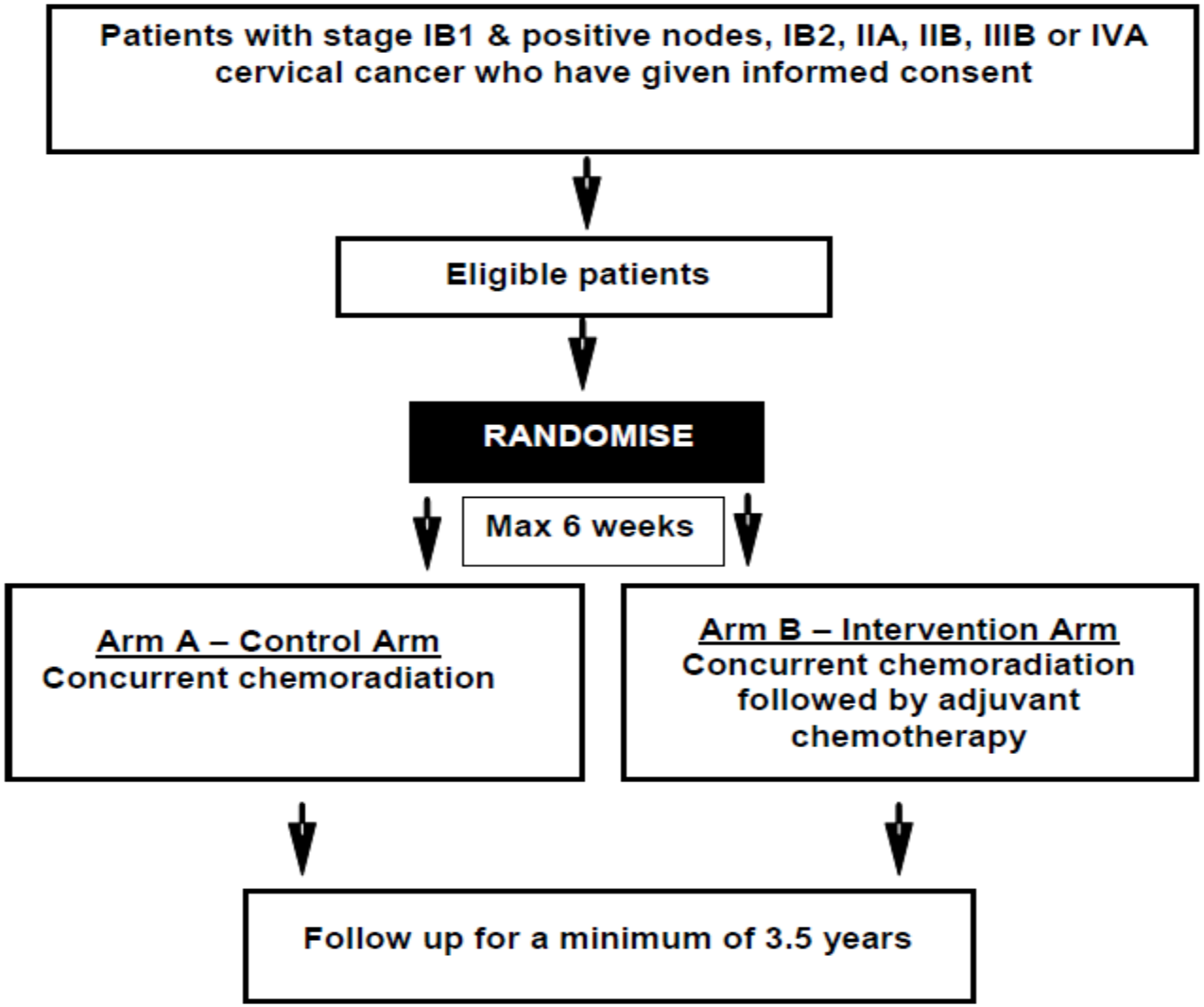


JCO meta-analysis suggested improved survival in the 2 trials that gave 2 cycles of additional chemo ('OUTBACK')

- may treat micromets and improve survival
- Absolute 5 year OS benefit of 19%

Chemoradiotherapy for cervical cancer meta-analysis collaboration: JCO 2008

Study Schema



OBJECTIVES

Primary objective: To determine if adding adjuvant chemo to standard chemo-XRT improves overall survival

A total sample size of 900 (450 per arm) will have 80% power with 95% confidence of detecting a reduction in the hazard of death of at least 32% (hazard ratio 0.68) from the control regimen

- looking for 8% improvement in overall survival at 5 years from 72% to 80%

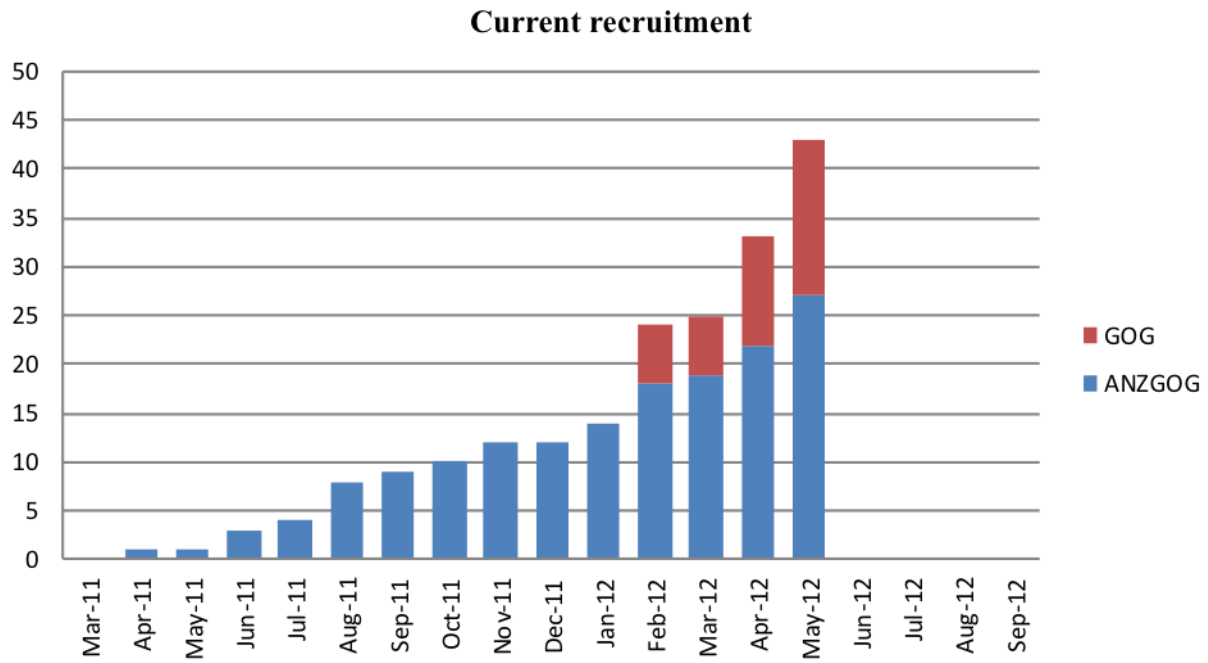
How OUTBACK evolved

- Originally presented at the ‘new concepts’ session at the ANZGOG (local Australian) meeting in 2008
- Proposed as a 40 patient phase II to assess feasibility and tolerability
- Protocol taken to local trial development workshop in 2009 by fellow
- Concurrently presented for discussion at the GCIG Cervix Consensus meeting in Manchester in 2009 and endorsed for further development as a phase III trial

The challenges

- Persuading PHARMA to supply paclitaxel
- Multiple unsuccessful Australian grant apps despite international interest
  - PeterMac, Perpetual, Victorian Cancer Agency
  - NHMRC/Cancer Australia 2009-10, 2011
  - ‘don’t think you can do it’
- Persuading the US GOG to join
- Contracts, insurance, lawyers
- Not being able to open in India or South America

TRIAL OPENED MARCH 2011

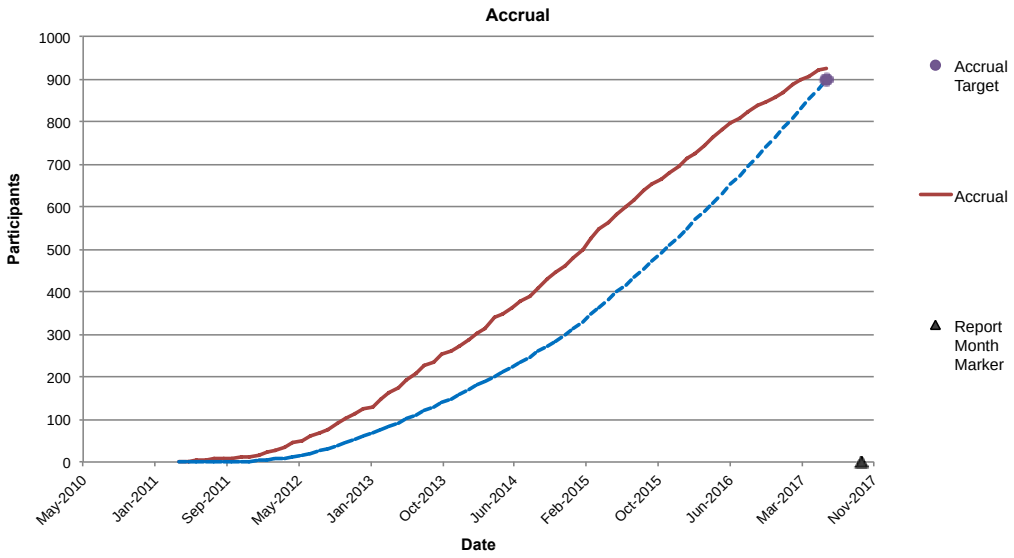


TRIALS OFTEN START SLOWLY!

The keys to success

- Lots of early morning teleconferences and thousands of emails
- Patience and diplomacy
- Think of it like running a marathon
- A great team of helpers and supporters locally
  - led by Julie Martyn from Sydney University
- Mentors – Martin Stockler, Danny Rischin
- Lots of international help and support
  Ted Trimble, Gillian Thomas, Bill Small
  Dave Gaffney, Kathleen Moore, Brad Monk
- Believe in yourself!

Completed recruitment June 2017



Country	Accrual
Australia	145
Canada	28
China	9
New Zealand	23
Saudi Arabia	5
Singapore	1
USA	715

So far about 2/3 of deaths needed to trigger analysis have occurred

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From little things…