



PaCCSC
Palliative Care Clinical Studies Collaborative

Tania Shelby-James
National Manager



Flinders University receives funding for PaCCSC from the Australian Government Department of Health and Ageing under the National Palliative Care Program.



Investigators

- David Currow
- Tania Shelby-James
- Debra Rowett
- John Plummer
- Geoff Gourlay
- Simon Eckermann
- Amy Abernethy



Funding

- Funded by the Australian Government Department of Health and Ageing under the National Palliative Care Strategy
- Funding period April 2007 – June 2010



Background



National Medicines Policy

4 central objectives

- Appropriate standards of quality, safety, efficacy (TGA)
- Timely access to, and affordable cost of medicines (PBAC)
- Quality use of medicines (clinical community)
- Maintaining a responsible and viable medicines industry (key partnerships)



Challenge to providing medicines for palliative care

- The medicine is not registered for supply in Australia
- The medicine is registered but not PBS listed
- The specific dosage, indication and formulation needs for administration to palliative care patients are not covered by the TGA or PBAC data
- The discontinuation of older or low usage medicines by manufacturers



Identifying priority palliative care medicines

- National priority setting which attempts to combine:
 - An assessment of need
 - An estimation of the likelihood of success
 - Resource requirements
 - The underlying values of those making the decisions
- National survey (2000)
 - For 25 most frequent symptoms
 - Key medicines used
 - Level of evidence
 - Current availability



Criteria to prioritise medicines for possible PBS listing

- Availability of data
 - Indication
 - Route of administration
- Wide consensus about use
- Magnitude of the problem
- Medicines that were likely to avoid hospitalisation
- No equivalent medicines already listed
- A number of palliative indications for the one medicine

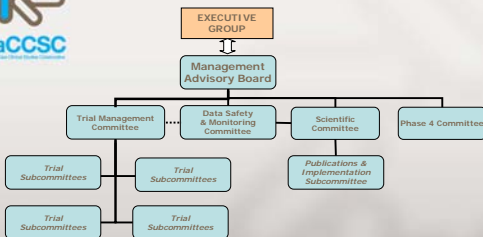


Progress to date

- Palliative care section with the PBS
 - Some medicines not previously PBS listed now available
- BUT**
- Medicines that remain on the PCMWG list do not have sufficient evidence to obtain PBS listing
- NEED**
- Rigorously designed prospective clinical trials at a level of quality that would allow the results to be used in registration and subsidy applications if positive



Palliative Care Clinical Study Collaborative PaCCSC



Structure

- Management Advisory Board
 - Chair: Prof Felix Bochner
- Scientific Committee
 - Chair: A/Prof Andrea Mant
- Trials Management Committee
 - Chair: Prof Janet Hardy
- Phase 4 Committee
 - Chair: Debra Rowett
- Data Safety Monitoring Board



PaCCSC

Structure

- Trial Subcommittees for each medicine being studied
 - Ketamine (Janet Hardy)
 - Risperidone (Meera Agar)
 - Ondansetron (James Stevenson)
 - Megesterol Acetate (Paul Glare)
 - Octreotide (David Currow)
 - Ketorolac (Odette Spruyt)
- Central management
- Site staff
 - Coordinator, consultant, study nurses – Phase 3
 - Coordinator – Phase 4



PaCCSC

Coordinating Centre

- Flinders University
- Based at the Repatriation General Hospital
- Staff
 - National Manager
 - Project Officer
 - Administration Officer



PaCCSC

Coordinating Site

- Overall study management
- Statistical management
- Financial management
- Administrative management
- Training of site staff on relevant legislation



PaCCSC

Scope of work to be done

- 6 initial sites/ investigators working in 5 states
- Prospective phase 3 clinical studies
- Prospective phase 4 pharmaco-vigilance studies on phase 3 medicines being studied
- Development of consumer impact statements on medicines being studied
- All studies to be completed by June 2010



PaCCSC

Current Phase 3 sites

- Selected by national consensus process
- NSW Cancer Centre, NSW
 - Braeside Hospital, NSW
 - Peter MacCallum Cancer Centre, Vic
 - Mater Adult Hospital, QLD
 - Southern Adelaide Palliative Services, SA
 - Western Australia Centre for Cancer and Palliative Care, WA



PaCCSC

Medicines being studied

- Ketamine for complex pain
 - Ketamine vs placebo
 - 5 day study
 - In-patients with chronic cancer pain
 - Haloperidol and/or Midazolam rescue
 - Primary outcome: average pain score at start of day 6
 - Sample size 150 patients



PaCCSC

Medicines being studied

- Risperidone for delirium
 - Risperidone vs Haloperidol vs placebo
 - 3 day study
 - In-patients with delirium
 - Midazolam rescue
 - Primary outcome: sum of scores on Nu-Desc scale items 2,3 and 4 at 72 hours
 - Sample size 165 patients



PaCCSC

Medicines being studied

- Octreotide for bowel obstruction
 - Dexamethasone, renitidine & octreotide vs Dexamethasone, renitidine & placebo
 - 72 hour study
 - Advanced cancer patients with bowel obstruction and vomiting that precipitates hospital admission or change in clinical care
 - Primary outcome: number of days without an episode of vomit
 - Sample size 92 patients



PaCCSC

Medicines being studied

- Megestrol acetate for anorexia
 - Dexamethasone vs megestrol acetate vs placebo
 - 1 week primary outcome with up to 4 weeks treatment if beneficial
 - Cancer patients with self-reported loss of appetite and weight loss
 - Primary outcome: appetite score at day 7
 - Sample size 210 patients



PaCCSC

Medicines being studied

- Ondansetron for cholestatic itch
 - Protocol still under development
 - Ondansetron vs placebo
 - Standardised skin care in both arms
 - 5 day study
 - People with intractable cholestatic itch
 - Promethazine rescue
 - Primary outcome: self-reported itch at day 5



PaCCSC

Design of phase 3 studies

- Randomised
- Double-blind
- Controlled
 - Current practice comparator
 - Placebo
- Health economic evaluation built into each study
- Efficacy end-point with effectiveness continuation



PaCCSC

Challenges for Phase 3 studies

- Will need to have multi-site recruitment
- Multiple Research Ethics Committees
- Not all sites may have the same level of research expertise
- Study designs must be sensitive to the needs of people with a life-limiting illness
- Maintaining enthusiasm over the length of the studies
- Recruitment, particularly in the complex studies



PaCCSC

Phase 4 studies

- Pharmaco-vigilance of specific symptoms studied in phase 3
 - Pain
 - Delirium
 - Anorexia
 - Cholestatic itch
 - Bowel obstruction
- Prospective
- Look at net benefit (benefit and burden)
- Reflect real world use of medicines



PaCCSC

Other work

- Effect of Dual listing of medicines in the PBS schedule
 - Palliative care specific pages and general pages
- Benzodiazepine use in palliative care
 - Audits to be conducted by phase 4 sites
- Patient impact statements to accompany any subsidy applications



PaCCSC

Achievements to date

- Established a working governance structure
- PaCCSC infrastructure in place –SOPs
- Contracts signed
- Literature reviews of key medicines
- Feasibility audit
- Scientific committee approval for 4 studies
- 1 trial currently recruiting
- Phase 4 pilot audit underway



PaCCSC

Acknowledgements

- Palliative Care Medicines Working Group, chaired by Professor Peter Ravenscroft
- Communications working group chaired by A/Professor Geoff Mitchell
- Department of Health and Ageing Palliative Care Branch