Minutes of the
Australasian Lung Cancer Trials Group Meeting
Crowne Plaza Hotel, Melbourne
Bridge Room 2
Friday 1st May 2015, 9.00am – 4.00pm

Present: T Ahilas (Maurice Blackburn), G Bannink, L Butler, L Cameron, M Chan, T Clay, C Cocks, H Dhillon, M Duffy, M Franco, V Ganju, F Hegi-Johnson, B Hughes, C Hunter, B Ivemy, T John, S Kao, J Kerr (Boehringer Ingelheim), C Lewis, A Livingstone, D Manners, S McCullough, S McLachlan, M Millward, P Mitchell (President, Chair), M Montealegre (MSD), A Reznichenko, G Richardson, A Rose, S Sampson, I Stubbin, N Van Zandwijk, C Vearing (MSD), R Woodfield (Novartis), A Woollett, S Yip.

Apologies:

Commenced: **9.10 am**

WHO	ACTION	COMPLETED
KL	Add viability of NZ rep to next MAC agenda	√

1. Welcome and Introduction

PM opened the meeting and welcomed attendees.

2. President's update

PM updated the group on the development of the International Trials Group advising that a Steering Committee has now been setup and two teleconferences have been held to date. The committee is organising a meeting at WCLC with NCIC to build the relationship and also meet with global and local industry to discuss upcoming trials that could be collaborated with a few countries as an initial trial for the International group.

3. Minutes of the previous meeting

The minutes of the previous meeting held on 15 October 2014 were considered a true and accurate record.

MOTION:

That the minutes of the meeting on 15 October 2014 be accepted as a true and accurate record of that meeting.

Moved: Haryana Dhillon ***Seconded:*** Michael Millward

4. Treasurer's Report

Cameron Hunter presented to the group and advised ALTG has improved their finances in 2014 with the main sources of income being the Cancer Australia infrastructure funding grant which ends 30 June 2016 and Cancer Institute NSW which ends December 2015. CH noted that if these grants are not available for re-application at the end of the funding period the group will struggle without the infrastructure support.

Additional income in 2014 for the group came from Industry Sponsorship $16,650 (BMS; MSD; Novartis; AstraZeneca; Maurice Blackburn; Boehringer-Ingelheim) and Research Infrastructure Block Grants $43,348. CH noted that the group has $110,767 in the non-expiring funds account which has grown from $54,449 (2013) to $110,767 (2014).

CH advise that the main areas of expenditure for the group in 2014 were (1) USYD Clinical Trial Centre Trials $816,384; (2) Trial Salaries $335,329; (3) Admin Salaries $101,876; (4) Meeting Costs $37,876; (5) Travel Grants $15,190

CH advised that it was important for the group to strategise for the future and the finance sub-committee will need to work on generating more income so the group doesn't rely heavily on infrastructure grants.

5. Secretary report

Michael Millward presented to the group and advised that the group currently has 471 members.

MM noted that when you breakdown the membership by discipline the medical oncologist, nurses and research fellow disciplines are the largest with the surgeons being one of the smallest and a discipline that needs to be targeted.

MM noted that the MAC had a New Zealand representative position vacant and if there were any members from NZ that would like to join the MAC. No NZ members volunteered so MM felt that the MAC should revise if a NZ member is necessary on the MAC.

ACTION: KL to add viability of NZ rep to next MAC agenda

6. ALTG Existing projects

ALTG 14/001 – BR31 (PI – Sue-Anne McLachlan)

- Sue-Anne McLachlan presented to the group the BR31 trial. ALTG was approached by NCIC to be the Australian group to coordinate the study.
- This study is a Phase III Prospective Double Blind Placebo Controlled Randomized Study of Adjuvant MEDI4736 in Completely Resected NSCLC. This is a multi-centre, prospective, RCT, double blind, placebo-controlled trial for patients with completely resected primary stage IB (≥ 4cm), II and IIIA NSCLC. It was noted that a QoL component has been included in the study by Prunella Blinman and Martin Stockler which is the preference study and a genomic database line has been included in the protocol.
- Sue-Anne advised that once the completely resected patient is registered, their tumour sample is sent to NCIC to check for PDL1 and then the patient is randomised for the study receiving either the drug or placebo. It was noted that adjuvant chemo needs to be discussed with all patients and must be documented. If patients have not received it they still will be included in the trial. The patient will receive it intravenously 1 hour infusion every 2 weeks for the first 6 months.
- The primary objective of the trial is to assess the impact of adjuvant therapy with MEDI4736 given by IV infusion for 1 year on the DFS of patients with completely resected (stage IB ≥ 4cm, stage II or IIIA), non-small cell lung cancer that is PD-L1 positive with the secondary objectives being:
    - DFS in all randomized patients
    - Overall survival for patients with NSCLC that is PD-L1 positive
    - OS for all randomized patients
    - Lung cancer specific survival for all PD-L1 positive patients and all randomized patients
    - Adverse effects and tolerability of MEDI4736
    - Quality of life

- Preferences
- Economic evaluation
- Evaluation of predictive/prognostic significance of PD-L1 expression
- Evaluation of changes in plasma/serum cytokines and other blood and tissue based biomarkers after treatment with MEDI4736 and at disease event
- Exploratory pharmacogenomic assays (baseline only

- There are 26 Australian sites: NSW (9); VIC (6); QLD (4); SA (2); WA (2); TAS (1); ACT (1) and 1 New Zealand site.
- Recruitment will be 200 patients from Australia and New Zealand and total recruitment being 1100 globally.
- The Royal Prince Alfred is the lead site with ethics approved. New Zealand is progressing, amendments have been made and will be approved this month – recruitment should start in June.
- The group were advised that tissue slides were mandatory and had to be sent to Canada. With the blinding of the placebo group, timelines are complicated to send tissue so a flowchart is currently being developed to assist centres.
- Tom John enquired about the rationale of using PDL+. Sue-Anne advised it was to see if it enhances treatment or not.

ALTG 13/008 – Investigating the impact of early palliative care (PI – Jaclyn Yoong)

- Nick Pavlakis advise that this study has submitted a funding grant to Cancer Australia which is pending approval.

ALTG 14/003 – MPM Study (PI – Steven Kao)

- Steven Kao advised that this was a phase II trial of nab-paclitaxel as second line chemotherapy for advanced malignant pleural mesothelioma.
- 1:1 randomisation nab-pac and gemcitabine vs abraxane alone. This is a two stage design with a 5-20% response rate
- Steven advised that he has met with Celgene who are keen to include Asian sites but they were concerned of the length of the trial.
- It was noted that there is the option of adding PDL1 treatment but this will need further discussion on the design and if PDL1 was included the protocol would need to be changed to 2 week scheduling.
- Ken O'Byrne had concern including PDL1 into the protocol with gemcitabine as it would increase the chance of pneumonitis. Data of concurrent treatments of immunotherapy before chemo gives better outcomes.

ALTG 14/002 – Phase II nivolumab + RT study in NSCLC (PI – Paul Mitchell)

- Paul Mitchell advised that this concept was discussed twelve months ago with BMS and Ken O'Byrne. This concept is a randomised phase II trial of nivolumab vs nivolumab plus radiotherapy in the treatment of advanced non-small cell lung cancer
- Paul advised that there currently is no data available for the combination of nivolumab with radiotherapy.
- It was noted that the primary endpoint is progression free survival at six months in non-irradiated tumour – 35% is not of interest but 50% is of interest.
- Eligibility criteria includes previously treated chemotherapy no more than 2nd or 3rd line and would include suitable extrathoracic lesion to irradiate.

- Feedback received from TROG was to include a QA to help assess toxicity.
- This study will be a multi-centre trial lead by ALTG and co-badged with TROG
- Paul advised that there is the potential of this study being an international trial for phase III.
- BMS has approved the budget.
- Michael Millward noted that there was a good clinical paper recently published on pembrolizumab and nivolumab.

7. ALTG industry sponsored session

Presentations were given by Theodora Ahilas from Maurice Blackburn and David Wanigesekera from Novartis. This item was not minuted.

8. ALTG Protocols for consideration:

CONCEPT: Randomized phase II trial of Afatinib with or without concurrent whole brain radiation therapy for EGFR mutant NSCLC with brain metastases (PI – Yu Yang Soon)

- Yu Yang Soon presented this concept to the group. The aim is to compare the effects of Afatinib with concurrent WBRT versus Afatinib alone on intracranial disease control.
- Hypothesis: Afatinib with concurrent WBRT will improve intracranial disease progression free survival at 6 months relative to Afatinib alone
- Inclusion criteria is: NSCLC with sensitizing EGFR mutations; brain metastases diagnosed de novo; not suitable for surgery or radiosurgery
- Nick Pavlakis presented his feedback asking is this a significant clinical problem? Yes as brain mets are a frequent site of drug failure in NSCLC adenocarcinoma (up to 50% incidence); higher baseline incidence in EGFR MT + NSCLC ~20%, similar cumulative incidence; and variable CNS activity of EGFR TKIs, but generally better therapy response (RT) than non mutated NSCLC
- Nick also noted that this was a sufficient clinical problem to justify the study, which is reasonably well designed if perhaps underpowered and would need RT input re RT standardization and patient selection
- Nick's main concerns were the standardizing patient selection (MDT or specific criteria excluding patients for SBRT); validation of RANO criteria as PE in metastatic disease setting; differential OS activity of afatinib in Exon 19 v Del Exon 21 probably needs to be considered; and 3rd Generation EGFR TKIs might make Q less important in the future
- The group agreed that this study proposed is a worthy one to pursue. It is hard to ascertain upfront but other studies advise could be up to 20% response rate.
- It was agreed that RT input was needed to discuss whether it would be better to give treatment up front rather than later on or do a non-comparative trial looking for a signal.
- Paul Mitchell noted that if it is 1st or 2nd line TKI and if the data suggest afatinib controls the brain mets than use.
- Michael Millward noted that it would be easy to build a safety review into the design. If this study is funded through industry it may become the preferred treatment for brain mets.
- Vinod Ganju suggested that it might be better starting with a small 1-2 site study intensively to build feasibility. This would mean you would get a rapid early response.
- Nick Pavlakis suggested using a new generation drugs. Tom John noted that the pre-clinical data for a new drug 3579 was very impressive.

- It was agreed that the group was interested in the question with the possibility of using newer therapies. ALTG wouldn't support the concept as it is but suggested to continue working on the idea and keeping the group updated.

CONCEPT: A randomised trial of adjuvant chemotherapy versus observation for resected T1-2aN0 pulmonary adenocarcinoma of solid predominant or micropapillary subtypes

- Tim Clay presented to the group a randomised trial of adjuvant chemotherapy versus observation for resected stage 1 pulmonary adenocarcinoma of solid predominant or micropapillary subtypes.
- The primary objective of this study is to demonstrate an improvement in DFS for T1-T2aN0 solid and micropapillary predominant tumours.
- Key Inclusions:
    - T1-T2aN0 solid predominant or micropapillary predominant AC
    - Minimum surgical procedure of lobectomy and adequate sampling of N1 and N2 nodes (negative EBUS or mediastinoscopy preop if required based on radiographic/PET findings)
    - Clear surgical margins
    - Usual inclusion/exclusion criteria for chemotherapy trials
- Stratification for randomisation
    - Tumour stage – T1a vs T1b vs T2a
    - Predominant subtype – solid vs micropapillary
- Tim advised that recruitment for this study was large
- Sue-Anne McLachlan presented her feedback on the study advising that there was room to further improve this protocol with more operations being done for stage 1 disease and introduction of screening it is more likely that these tumours will be seen.
- It was also noted that molecular factors might be in competition to this study.
- Nick Pavlakis summarised and suggested that this concept needs to further work on recruitment numbers and involve a surgeon to enquire what the surgical question should be. The group could work this study in parallel with companies that are willing to pay sponsorship. Nick noted that input from a pathologist would be needed.
- It was agreed that further discussions would be held at ASCO with Ken O'Byrne, Nick Pavlakis and Paul Mitchell willing to assist in the development of this protocol.

CONCEPT: Abraxane Maintenance in SCLC

- Paul Mitchell presented to the group a randomised phase II study of switch maintenance nab-paclitaxel plus BSC vs BSC alone in extensive-stage small cell lung cancer non-progressive after initial platinum-based chemotherapy.
- Primary endpoint is progression free survival.
- Paul noted that he is requesting that ALTG lead the study. Paul also noted that Celgene has been very supportive of this idea.
- Paul noted that he sees the role of ALTG working with Asian sites and groups and would like for this to happen.
- Initially it will be a phase II trial with the possibility of it being a phase III study later on.
- Michael Millward presented feedback noting that this was a significant issue and this is a problem of concern for the group.
- Michael noted that the rationale to do this study was sound with a lot of studies done in the past with most of them involving sequencing of chemotherapy, they found toxicity, found

small PFS, no change of practice. More recently studies that are non-toxic which was negative. Not aware of this type with immunotherapy. Not a high priority

- Michael noted that it was useful data to use with plenty of data using the parallel drug.
- Michael felt that the endpoint was adequate and progression free survival is reasonable if not blinded will be an exploratory study and turn into phase III
- Michael noted that it was a feasible study, that you could accrue 150 SCLC patients
- Funding has been sought from Celegene
- Michael noted that excluding a patient with brain mets could be costly scanning every patient before they start.
- Potential to change practice – no but would lead to a bigger study and enrich the literature
- Add on possibilities – interest on SPARK
- Possibility for future research opportunities
- Michael felt that this study would be good to establish a SCLC trial
- Vinod Ganju suggested using drugs such as hedgehog inhibitor rather than immunotherapy. Could look at promising new agencies. Difficult patients to recruit. Michael noted that you could spend a lot of time on a path inhibitor with the hedgehog inhibitor being very poorly tolerated when given to patients

<u>CONCEPT: TOPDOSE - Dose Adjusted Platinum-Based Chemotherapy for Advanced NSCLC (PI – Rina Hui)</u>

- Matthew Chan presented the Topdose concept to the group. This is a Dose Adjusted Platinum-Based Chemotherapy for Advanced Non-Small Cell Lung Cancer study.
- Matthew advised that the aim was to determine the activity of dose-adjusted chemotherapy (carboplatin/gemcitabine) based on nadir neutrophil count in patients with locally advanced or metastatic NSCLC.
- It was advised that the primary endpoint was progression free survival at 6 months in the dose-adjusted arm (imaging, RECIST 1.1) with the secondary endpoint being disease control rate (CR + PR + SD); survival at 12 months in the dose-adjusted arm (death from any cause); overall survival (death from any cause); adverse events (CTCAE v4.03); health related quality of life (HRQoL)
- The feasibility is that it is a pragmatic study, as commonest first-line chemotherapy regimen for advanced NSCLC in Australia is carboplatin / gemcitabine; Study procedures mostly consistent with standard care.
- At the end of this randomised phase II study consideration can be made whether to undertake randomised phase III study. This phase II study will inform patient numbers required for phase III study
- It was noted that funding was sought from BUPA without success and co-operative group support is being sought from ALTG.
- It was noted that this study requires submission of a grant application to Dust Diseases Board, Cancer Australia or NHMRC
- Brett Hughes presented to the group his feedback on this study noting that some changes/ questions need to be considered before it goes ahead:
    - Need to remove variables/inconsistencies in design <100 pts receiving intervention
    - Optional Dose modifications and cycle number
    - Remove 20%DR for PS 2 and >75 y.o.
    - Pick 4 OR 6 cycles for entire study

- Unfortunately, decision re: maintenance chemo needs to be mandated in protocol – not optional
- →4 cycles platinum double then maintenance Pem

- Additional issue of capped PBS Pemetrexed dosing - How will this fit into a TOPDOSE design if incorporated?
- Brett noted that the methodology should be less flexible and specify up front which treatments people can take.
- A decision needs to be addressed about maintenance chemotherapy – using 4 cycles
- Brett noted that this was an excelledt study but funding will be a big issue
- Michael Franco suggested that a QoL question be included as it is interesting data being collected. Haryana Dhillon also suggested taking blood to look at a neuropathy QoL question

<u>CONCEPT: Multi-centre pilot screening trial into early detection</u>

- David Manners presented to the group his study idea noting that the benefits of screening high risk individuals with low dose CT (LDCT) reduces lung cancer mortality by 20%
- David noted that the 2014 ALCC held in Brisbane held a meeting to further discuss lung cancer screening with the suggestion that this group be under the umbrella of ALTG.
- David noted his conflict of interest receiving funding for my fellowship is provided by the WA Cancer and Palliative Care Network through the Department of Health WA funding from Western Perth.
- 55,000 screening people at high risk. Lung cancer screening is recommended in US and is funded by US with 11% over dosage rate.
- It was noted that 1500 people over 4 sites is proposed with the sites being TPCH SCGH, Royal Melbourne Epworth and a regional centre in Bunbury.
- David requested from the ALTG to provide the following services:
- Assist grant and funding applications
  - Budget development
  - Provide independent study support and oversight
  - Assist liaison with Department of Human Services
  - Use Medicare database to identify participants
  - Develop, house and manage study registry
- Michael Millward recommended to contact an ALTG consumer to provide input and also a general practitioner such as Jon Emery. David Manners advised that he is working with Andrew Bowen and another consumer based in WA.

9. Consumer Update:

Ian Stubbin presented what the consumer group can do for ALTG. Ian queried if life expectancy was the only important question of a trial or is it QoL. Ian advised that the consumers lobby and identify sources of funding. The benefit of having a consumer group is that these people come from widely varied backgrounds and that there were not a lot of lung cancer consumers.

Haryana Dhillon queried the membership on how the consumer group could work more effectively with clinicians. Was is due to a lack of understanding on how to go about engaging consumers most effectively.

Haryana also noted that if there was interest from the members the consumer group would look at the possibility of holding a workshop improving and guiding on how clinicians can work together with consumers.

10. ALTG industry sponsored session

Presentations were given by Chris Vearing from MSD and Liza Regalado-Tram from AstraZeneca. This item was not minuted.

11. Idea Generation Workshop (IGW)

Working Group 1: Advanced NSCLC (1st line systemic therapies)
Group Chair: Brett Hughes, Medical Oncologist, Prince Charles Hospital, Brisbane
Group Attendees: PM, MM, Craig Lewis, Anthony Linton, Chris Cox, Ken O'Byrne, Ben Solomon, Matthew Chan, Laura Butler, Annette Tognela

Plenary discussion:

Idea 1: Platform study (Master protocol)

- Clinical problem: How to design and conduct trials for rare mutations in NSCLC which would be recognised and accepted by PBS for future funding applications.
- Proposed intervention: Platform diagnostic with New Oncology
- Suggested trial: widespread genomic testing and targeted treatment of rare mutations (ROS1, MET, RET, HER2, BRAF etc) vs chemotherapy
- Phase of development: 2/3
- Primary endpoint: PFS and/or OS
- Comment by PM: to be competitive in the international arena this idea is a great way to start to setup an international study

Idea 2: Sequencing of immunotherapy and chemotherapy

- Clinical Problem: Optimal sequencing of immunotherapy, immune priming, tumour antigen presentation
- Proposed intervention: Chemotherapy and immunotherapy
- Suggested trial: 4 cycles of chemotherapy then immunotherapy vs 4 cycles of immunotherapy then chemotherapy (irrespective of response)
- Phase of development: 2/3
- Primary endpoint: PFS

Idea 3: Duration of immunotherapy

- Clinical Problem: Duration and frequency of immunotherapy is unknown
- Proposed intervention: Immunotherapy
- Suggested trial: Run-in immunotherapy alone and then continued vs intermittent dosing. This trial could be run as first or subsequent line of therapy
- Phase of development: 2
- Primary endpoint: PFS

Idea 4: PARP maintenance trial

- Clinical Problem: Homologous repair deficiency tumours
- Proposed intervention: PARP +/- EGFR TKI or ALK TKI
- Suggested trial: PARP maintenance post TKI
- Phase of development: 1/2
- Primary endpoint: safety, PFS, response rate

Working group discussion (supplementary notes)

Idea 1: Platform study (Master protocol)

- Concept proposed by Brett Hughes
- Ros1, BRAF, MET etc – how to design a trial to cover all rare mutaitons which would be acceptable to PBS going forward. Require collaboration with pharma and companion diagnostics.
- US Master-protocol – think this set up as 2nd line. Other models – Europe, Foundation Medicine, New Oncology (Cologne).
- Funding - Cancer Australia seems keen in terms of testing. GCCTI has funding to write a protocol available.
- Discussed whether could link to rare tumours group (?David Sweeney). It may be possible to use molecular profiling as a platform (joint initiative) for other tumour streams. Alternatively, could use for rare tumours + eg, larger mutation group (EGFR) with new agents.
- Perhaps concept could be extended to all lines of treatment. First line may be problematic given turn-around times.
- Who is doing testing – Peter Mac, other centres?
- Design – platform alone or therapeutics incorporated study? Potential phase 2 of rare mutations to be lined up.
- Consider pharma companies – perhaps have platform established and then pharma able to approach to add on studies (likely start as phase 2 then roll into phase 3)
- Possible 1 centre for each state doing each trial
- What makes Australia attractive for pharma? Potentially rapid approval by TGA.

Idea 2: Sequencing of Immunotherapy and chemotherapy

- Concept proposed by Ken O'Byrne
- Immunotherapy priming for chemotherapy. What is the optimal sequencing of chemotherapy and immunotherapy?
- Preliminary discussion with BMS at ELCC – potentially global study/collaborative
- 4 cycles of nivolumab then chemo or chemo then nivo – irrespective of response
- Phase 2 data showing significant improvement in OS
- Dr Ramalingum also interested
- Perhaps only small number of centres involved
- International trial collaboration

Idea 3: Duration of immunotherapy

- Concept proposed by Ken O'Byrne
- Immunotherapy – run-in period of immune therapy alone then continued versus intermittent doses of immunotherapy
- If pembro and nivo funded, possibly seek govt funding for study re duration and frequency of treatment. Some evidence that cell receptors saturated after 1 dose of nivo so potentially only need 3 monthly treatment.
- Short term funding is main issue.
- Potentially align with front runners or even those centres lagging behind.

Idea 4: Immunotherapy in mutated NSCLC

- Concept proposed by Ken O'Byrne
- Potentially have a trial of immune therapies upfront with EGFR or other mutations in NSCLC (eg, RAS tumours)
- Studies underway

Idea 5: EGFR 19 mutation or ALK rearrangement + PARP

- Testing of tumours for homologous repair deficiency
- Proposed intervention: EGFR + PARP inhibitor 2nd line (maintenance or concurrent)
- Pharma interested

Idea 6: Maintenance PARP

- Proposed intervention: Maintenance PARP in pts who respond to treatment
- Look for BRCA-ness in germline
- Could be used in NSCLC and meso studies.

Working Group 2: Advanced NSCLC (2nd line systemic therapies)

Group Chair: Dr Tom John, Medical Oncologist, Austin Hospital, Melbourne
Group Attendees: Nick Pavlakis, Tim Clay, Vinod Ganju, Steven Kao, Mark Donoghue, Subotheni Thavaneswaran, Nico Van Zandwijk

Plenary discussion:

Idea 1: Biomarkers in primary chemo-refractory, non-mutated NSCLC

Tom John presented the idea which is summarised below:

- Background – it is a difficult space as there are a lot of pharma driven studies. EGFR and ALK studies wouldn't be ideal to propose. Immune studies using Nivolumab have potential but there are a number of 2nd line trials already in progress.
- Target population - patients with primary progressive disease
- Aim - Identify genotypic characteristics amongst this group that can be prospectively validated and perhaps linked to particular phenotypic characteristics that can help us identify these pts and alter their management upfront
- NLR (neutrophil to lymphocyte ratio) was discussed as a potential biomarker and whether it is predictive of those more likely to develop primary progressive disease. Issues with NLR are the absence of validated cut-offs for the ratio and the effect of steroids on NLR. The concept is based on a recent Cancer Immunology paper by Naiyer A Rizvi et al. A prospective observational cohort study of patients with non-oncogene driven NSCLC.
- Methods - Patients would consent to tissue and blood collection at baseline (prior to exposure to any chemotherapy). Amongst those with progressive disease, a further blood test and tumour sample would be taken to assess for changes in potential predictive/ prognostic markers that demonstrate a unique pattern – eg, LDH, NLR which may then be correlated with clinical characteristics – ECOG/ symptoms.
- 2nd line treatment would not be defined in the trial (Investigator choice) and may include chemotherapy, EGFR TKI, immune therapy, or no further treatment. Clinical outcomes based on treatment received will be linked to changes in these potential biomarkers in blood and/or tissue.
- This would create a tumour registry stratifying patients based on these biomarkers to clinical trials with therapies that are most appropriate for them and the features specific to their cancer.

Feedback on Idea 1:
Brett Hughes – agreed that the field in 2nd line trials was saturated but the proposed idea would provide a framework to understand the genomics of patients that don't respond to chemotherapy. NP – could use trial to gather information, and set up a register. Enrolment onto this "biobank" project would not preclude going onto a trial and recruitment would be easy.

Working Group 3: Diagnostic/Screening/Prevention/Surgical
Group Chair: Dr Cameron Hunter, Respiratory physician, Wyong Hospital
Group Attendees: Sonia Yip, Ann Livingstone, Sandy Sampson, Ian Stubbin, David Manners, Alex Dobrovic, Anand Rose, Sue McCullough

Plenary discussion:
Idea 1: Sub-study of screening trial - sample processing
- Suggest parallel trial/sub-study of screening trial (proposed by David Manners) assessing consistency of methodology for collection and processing of biological samples.
- This sub-study could be available to limited sites participating in the screening study.
- The group proposed ALTG consider setting up a standard process for blood taking and processing common to all their trials.

Idea 2: Adequacy of EBUS needles for biopsy
- In context of PDL1 testing, adequacy of EBUS needles for biopsy compared to FNA-biopsy, core biopsy etc for tumour sampling
- Also discussed EBUS compared to tumour resection specimens regarding the quality of samples obtained
- Need to ensure this process is adequate to save 2nd procedure and possible comparison of new EBUS core needle (only used in last 12 months so lack of data)
- Cost of new needles also discussed

Idea 3: Radiotherapy vs surgery
- Anand Rose suggested – Revisiting and refining the decision making in radiotherapy v surgery and the role of PET in potentially operable lung cancer

Working group discussions (additional)
- Epigenetics - could provide possible therapeutic future opportunities (eg, may be important in EGFR). The group discussed methodology and the most amenable example (eg, DNA methylation).
- Circulating DNA – able to monitor tumour progression prior to changes being identified on a scan. There are limits of detection re amount of DNA shed into circulation depends on tumour size. Blood is easy to collect but it is important that samples are processed correctly (i.e. must be spun twice etc).
- Smoking cessation - use of a quit smoking intervention in David Manners screening trial was discussed. In particular, the impact of smoking cessation on a screening program.

Working Group 4: Symptom control/Palliative care
Group Chair: Dr Michael Franco, Palliative Care physician and Medical Oncologist, Monash Hospital
Group Attendees: Haryana Dhillon, Glenda Colburn, Mary Duffy, Anne Woollett, Beth Ivemy, Sue Anne McLachlan, Guy Bannink

Plenary discussion:
Idea 1: Opiates and cough in lung cancer patients
- Following on from last year's IGW, update on pilot study in 38 pts at a single centre using methadone in the management of cough in lung cancer patients.

- Patients often already on opiates - will have low dose methadone as NMDA receptor blockade is important in the pathogenesis of the cough reflex.
- Primary endpoint - change in cough score and patient reported symptoms.
- Pilot study is due to open in mid-2015. Aim to expand to national, multi-centre study in ?2017.

Idea 2: Cachexia in lung cancer patients

- Rationale - David Currow worked on an appetite stimulation study which was a positive study.
- Suggest review of cachexia data and liaise with Cindy Tan/Nicole regarding what they are doing … possibility of assessing prognostic/predictive measures.

Idea 3: Attitudes of older patients to lung cancer and prognosis

- Attitudes of older patients when diagnosed with lung cancer is not known. Further, assessment of geriatric patients with cancer not well established. Communication with older patients is also an issue for clinicians. Could take to PoCOG.
- Rationale is nothing specific for healthcare providers in lung cancer regarding education and communication with the older lung cancer patient.
- Aim is to identify older patient's priorities and how to communicate with them.

<u>Comments at plenary:</u>

- Strategy of group is to fill gaps
- NP – ALTG to supply a pathway to assist members to develop an idea into a protocol.

<u>Working group discussions (additional)</u>

- Discussion opened based on where things left off at the end of IGW in 2014.
- **Causes or predictors of cachexia in thoracic malignancy** – discussion of whether cachexia is still relevant or whether intervention study is warranted? Nationally, there is a bit being done for cachexia. Recommended doing a structured literature review for areas of interest (?ALTG research fellows). Have a look at what others are doing. Suggest linking Nicole ?Kiss and Cindy Tan to see what studies could be undertaken.
- **Physical activity in lung cancer**. Currently, Tiger study underway at RMH just opening in Peter Mac looking at physical activity in the home. All oncology patients up to stage 3B included. Linda/Hary could review literature to see what has been done and combine outcomes.
- **Opiates and cough in thoracic cancer** – lack of data at present. Methadone has interesting data and effective on cough reflex. Idea was discussed last year at IGW of methadone vs placebo in people with malignancy and cough. Idea of small cohort using methadone v placebo with wash out period. Funded – plan now is to recruit 38 pts and run a single centre study (pilot). If benefits shown, then larger multi-centre study to compare morphine v methadone. Discussed looking at effect on cough, blood levels of methadone, two day wash out, check if blood levels of methadone have effect on cough. Methadone has negative stigma – looking at subjects attitudes also.
- **Fever & night sweats** – not sure what to do with it!!! Leave it here.
- **Frailty and cancer in the older persons**
  - Geriatric assessment score utility. Some studies show benefit, others don't. Issue is how do we assess the frail patient? Eg, is a frailty score important when surgery is considered? Bianca's study is doing the assessment before MDM presentation and comparing outcomes – but difficult as unknown - charts not read. COSA work is still being done in this area. Interventions for older patients – still in ethics process. **Hary** to find out more. European research in this area – eg, British trial published

yesterday showing benefit but how useful or translational is this? All agreed that we are seeing more older patients and need to look at this.
    - Presentation by Heather Lane (WA) at COSA regarding assessing geriatric patients.
    - Clinician's attitude to older people – choosing treatment/access to treatment. What we need is educational material for healthcare providers on how to talk to their older patients. Disconnect between what the doctor says to what the patient wants to, or does, hear. Skills training learned in teaching – does it appear in health literature? Interesting to find out what older patient's wishes are to lung cancer treatments.
- **Referrals/attitudes to lung cancer -** There is nihilism in primary care regarding lung cancer. John Emery has done some work on referral patterns. GP survey being undertaken. **ACTION**: Circulate the Stigma/Nihilism Cancer Australia report.
- **Mental health -** is an area to think about – lung cancer patients have higher rates of anxiety/depression. Suzanne Chambers has done some work in this area.
- **QOL Data collection** – Possibility of using app to collecting the data – QOL data on a reliable source.

PM closed the meeting at 3.20pm, thanking all for their participation.

Signed .....
Chairman

Dated: