

AUSTRALASIAN LEUKAEMIA AND LYMPHOMA GROUP (ALLG)

(ABN 96 066 593 100 / ACN 066 593 100)



ANNUAL RESEARCH REPORT FOR 2000

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FOREWORD

This is the first research report to be prepared by the Australasian Leukaemia and Lymphoma Group (ALLG), and it is our intention that this will be an annual exercise to summarise and highlight our research achievements each year. This first report describes the activities of the Group since its formation in May 1999, and provides an overview of its diverse clinical research programs.

A history of the formation of the ALLG from the Australian and New Zealand Lymphoma Group and the Australian Leukaemia Study Group is provided on the next page. The ALLG has been formed on the basis of the strong foundation of these two clinical trials groups, both with internationally recognised track records of innovative research in leukaemia and lymphoma, and has undertaken to enhance this record of achievement. Major studies in the treatment of acute myeloid leukaemia, intermediate grade non-Hodgkin's lymphoma, promyelocytic leukaemia, and other blood malignancies were carried forward as part of the legacy of the ANZLG and ALSG, and are discussed in this report. A variety of significant studies in other diseases are also described. These studies include those conducted by the Australasian Bone Marrow Transplant Cooperative Study Group, recognising the close association between stem cell transplantation and other forms of treatment for leukaemia and lymphoma.

As a result of the merger of the Australian and New Zealand Lymphoma Group and the Australian Leukaemia Study Group, a considerable reorganization of the operations of clinical trials activities has been required to allow efficient operation of the ALLG. A Trial Subcommittee structure has been created to "decentralize" the responsibility for the management of studies in particular disease categories. ALLG members with specific expertise and experience in particular diseases have been appointed to take charge of research activities in those areas, and to promote the general goals of the group in their respective fields. New proposals for studies will in future will be channelled through these Trial Subcommittee chairmen, who will be responsible for the overall direction of research in their area of interest. Representation of the Trial Subcommittee chairmen on the Executive Committee of the ALLG will ensure that the trials activity in their area of interest is adequately represented within the Group.

The ALLG is the major agent of clinical research in malignant diseases of the blood in Australia and New Zealand, and continues to expand its activities. A number of major collaborations with other international trials groups are an emerging feature of its activities. In addition, close relationships with major international pharmaceutical companies provide both opportunities and challenges. The interaction with these companies, and in particular the opportunities to gain access to exciting new drugs with activity in blood cancers, is the major challenge facing the ALLG.

Ken Bradstock
ALLG Chairman

HISTORY OF ANZLG AND ALSG

The Australasian Leukaemia and Lymphoma Group was formed in 1999 as a merger of the activities of 2 established clinical trials organizations, the ANZLG and the ALSG. As a result, the ALLG builds on the established reputations of the 2 groups.

The **ANZLG** was founded in 1973, and was initially developed as a collaborative group to investigate combination chemotherapy for intermediate grade non Hodgkins lymphoma. ANZLG was led by Dr. Ian Cooper for many years, then by Dr. Max Wolf. Membership in 1998 consisted of 159 clinicians, including haematologists, medical oncologists, and radiation oncologists. A pathology review panel was created to provide histopathology expertise for clinical studies, initially convened by Dr. Philip Ironside, then by Dr. David Ellis. The statistical and central data collection services for the ANZLG were based at the Trial Centre at the Peter MacCallum Cancer Institute in Melbourne, headed by Dr. Jane Matthews.

The publication record of the ANZLG attached at the end of this report summarizes its achievements. Major themes of research include early studies of the value of the podophylotoxin drug Teniposide in NHL; a large multicentre trial of MACOP-B compared to CHOP chemotherapy in intermediate grade NHL; an investigation of the role of Cladribine in low grade NHL; and most recently a large randomised trial of intensified chemotherapy for NHL. ANZLG participated in international cooperative studies with the Canadian National Cancer Institute, GELA, the European Bone Marrow Transplant Group, the European Organization for Research and Treatment of Cancer, and the British National Lymphoma Group.

The **ALSG** was formed in 1982 and initially focussed on studies in adult acute myeloid leukaemia. The group was initially led by Dr. Ray Lowenthal, then by Dr. James Bishop, and finally by Dr. Ken Bradstock. By 1998, ALSG had 120 members, predominantly haematologists, representing 48 centres. ALSG shared the same clinical trials facilities at the Peter MacCallum Cancer Institute as the ANZLG.

The ALSG conducted 2 major multicentre studies in AML between 1983 and 1991, which examined the role of intensification of induction chemotherapy. Both studies are now widely cited in the international literature on AML. ALSG also took a prominent role in the introduction of All Trans Retinoic Acid in the treatment of promyelocytic leukaemia in Australia, as well as Cladribine in the treatment of chronic lymphocytic leukaemia. International collaborations were established with European groups for trials in adult acute lymphoblastic leukaemia and CLL.

ELECTED MEMBERS OF ALLG EXECUTIVE COMMITTEE IN 2000

CHAIRMAN

Associate Professor Ken Bradstock

Westmead Hospital, Sydney

VICE CHAIRMAN

Dr. Max Wolf

Peter MacCallum Cancer Institute, Melbourne

SECRETARY

Associate Professor Peter Browett

University of Auckland, New Zealand

TREASURER

Dr. John Seymour

Peter MacCallum Cancer Institute, Melbourne

DIRECTORS

Professor David Ma

St. Vincents Hospital, Sydney

Dr. Timothy Hughes

Royal Adelaide Hospital, Adelaide

Dr. Paula Marlton

Princess Alexandra Hospital, Brisbane

Associate Professor Jeffrey Szer

Royal Melbourne Hospital, Melbourne

TRIAL CENTRE STAFF

ALLG BIOSTATISTICIAN

Dr. Jane Matthews

Statistical Centre, Peter MacCallum Cancer Institute,
Melbourne

ALLG CLINICAL TRIAL CO-ORDINATORS

Ms Janey Stone

Ms Heather Baxter

TRIAL CENTRE CONTACTS

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ALLG TRIAL SUBCOMMITTEES

INTERMEDIATE AND HIGH GRADE NON-HODGKINS LYMPHOMA, HODGKINS DISEASE CHAIRMEN

Dr. Max Wolf
Prof. David Ma

MYELOPROLIFERATIVE DISEASE, MYELOYDYSPLASIA CHAIRMEN

Dr. Timothy Hughes
Assoc. Prof. Kerry Taylor

LOW GRADE NON-HODGKINS LYMPHOMA, MYELOMA, CHRONIC LYMPHOCYTIC LEUKAEMIA CHAIRMEN

Dr. John Seymour
Assoc. Prof. Peter Browett

ACUTE LEUKAEMIA CHAIRMEN

Assoc. Prof. Ken Bradstock
Dr. John Seymour

BONE MARROW TRANSPLANTATION CHAIRMEN

Assoc. Prof. Jeffery Szer
Assoc. Prof. Ken Bradstock

LABORATORY SCIENTIFIC COMMITTEE CHAIRMEN

Dr. Paula Marlton
Assoc. Prof. Harry Iland

PUBLICATIONS of ANZLG and ALSG

AUSTRALIAN LEUKAEMIA STUDY GROUP PUBLICATIONS

1. Bishop J, Joshua D, Lowenthal R, Kronenberg H, Whiteside M, Cobcroft R, Dodds A, Wolf M, Manoharan A. A phase I-II study of cytosine arabinoside, daunorubicin and VP16-213 in adult patients with acute non-lymphocytic leukaemia. Australian Leukaemia Study Group (ALSG). Aust NZ J Med, 16:48-51, 1986.
2. Lowenthal RM, Chesterman CN, Griffiths JD, Manoharan A, Harris MG, Herrman RP, Rooney KF, Rozenberg MC, Salem HHH, Wolf MM, Woodruff RE. Oral idarubicin as a single-agent treatment of acute nonlymphocytic leukemia in poor-risk patients. Cancer Treatment Reports, 71:1279-1281, 1987.
3. Lowenthal RM. A possible special role for oral idarubicin in the treatment of leukemia following myelodysplastic syndrome. In: Mandelli F, Polli E, Clarkson B, Ganzina F, eds. 4th International Symposium on Therapy of Leukemia, Rome February 7-12, 1987: Proceedings of the session in idarubicin in the treatment of acute leukemia. Amsterdam: Excerpta Medica, pp50-55, 1987.
4. Bishop JF, Lowenthal RM, Joshua DE. Prospects for cure in acute leukaemia. J Clin Path, 42 (3):332, 1989.
5. Bishop JF, Lowenthal R, Joshua D, Wolf M. Etoposide in acute myeloid leukaemia. Leukaemia Res, 42:332, 1989.
6. Bishop JF, Lowenthal RM, Joshua D, Matthews JP, Todd D, Cobcroft R, Whiteside M, Kronenberg H, Ma D, Dodds A, Herrmann R, Szer J, Wolf MM, Young G. Etoposide in acute non-lymphocytic leukaemia (ANLL). Blood, 75: 1, 1-6, 1990.
7. Bishop JF. Etoposide in the management of acute leukaemia: A review. Semin. Oncol, 18 (suppl.2):62-65, 1991.
8. Bishop JF, Lowenthal RM, Joshua D et al. Etoposide in acute non-lymphocytic leukaemia. Haematology Digest, 5:13-14, 1990.
9. Bishop JF, Joshua DE, Lowenthal R, Wolf M. Etoposide in Leukaemia. Cancer, 67:285-291, 1991.
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11. Bishop JF, Lowenthal R, Joshua D et al. Etoposide in Leukaemia. Year Book of Hematology (in press), 1991.
12. Bishop JF. Etoposide in the Management of Acute Leukaemia. Semin Oncol, 19,6:1-6, 1992.
13. Lowenthal RM. Idarubicin. A new effective drug for treatment of adult acute myeloid leukaemia. Australian Journal of Hospital Pharmacy, 24:159-164, 1994.
14. Joshua D, Wolf M, Matthews J, Tan L, Sheridan W, Pilkington G, Page F. Peripheral blood surface antigen expression and prognosis in myeloma. Leukemia and Lymphoma, 14:303-309, 1994.

15. Bishop JF, Matthews JP, Young G, Szer J, Joshua DE, Dodds A, Laidlaw Cr, Cobcroft R, Herrmann R, Ma D, Page FJ. The influence of induction chemotherapy dose and dose intensity on the duration of remission in acute myeloid leukaemia.. *Leukemia and Lymphoma*, 15:79-84, 1994.
16. Bradstock K, Matthews J, Benson E, Page F, Bishop J, and the ALSG. Prognostic value of immunophenotyping in acute myeloid leukaemia. *Blood*, 84:1220-1225, 1994.
17. Coghlan D, Morley A, Matthews J, Bishop J. The incidence and prognostic significance of mutations in codon 13 of the N-ras gene in acute myeloid leukaemia. *Leukemia*, 8:1682-1687, 1994.
18. Wiley JS, Firkin FC, for the ALSG. Reduction of pulmonary toxicity by prednisone prophylaxis during all-trans retinoic acid treatment of acute promyelocytic leukaemia. *Leukemia*, 9:774-778, 1995.
19. Bishop J, Matthews J, Young G, Szer J, Gillett A, Joshua D, Bradstock K, Enno A, Wolf M, Fox R, Cobcroft R, Herrmann R, Van Der Weyden M, Lowenthal RM, Page F, Garson OM and Juneja S. A randomized study of high dose cytarabine in induction in acute myeloid leukaemia. *Blood* 87:1710-1717, 1996.
20. Bishop JF, Young GAR, Matthews JP, Bradstock KF. Induction endpoints in AML. *Blood*, 88:754-755, 1996.
21. Joshua DE, Penny R, Matthews JP, Laidlaw CR, Gibson J, Bradstock K, Wolf M, Goldstein, D. Australian Leukaemia Study Group Myeloma II: a randomized trial of intensive combination chemotherapy with or without interferon in patients with myeloma. *Brit Jnl Haem*, 97:38-45, 1997.
22. Bishop JF, Matthews JP, Young GA, Bradstock KF, Lowenthal RM. Intensified chemotherapy with high dose cytarabine and etoposide in acute myeloid leukaemia: a review with updated results. *Leukemia and Lymphoma*, 28:315-327, 1998.
23. Lowenthal RM, Bradstock KF, Matthews JP, Bishop JF, Cobcroft R, Eliadis P, Enno A, Gill D, Herrmann RP, Manoharan A, Page FJ, Rooney K, Rosenfeld D, Seldon M, Taylor KM, Wolf MM, Young GAR. A Phase I/II study of intensive dose escalation of cytarabine in combination with idarubicin and etoposide in induction treatment of adult acute myeloid leukemia. *Leukemia and Lymphoma*, 34:501-510, 1999.
24. Matthews JP, Bishop JP, Young GAR, Bradstock KF, Cobcroft R, Dodds A, Enna A, Garson OM, Gillett A, Herrmann R, Joshua D, Juneja S, Lowenthal RM, Ma D, Szer J, Taylor K, Wolf M. Patterns of failure with increasing intensification of induction chemotherapy for acute myeloid leukaemia, *Brit Jnl Haem*, 2000, in Press.
25. Effects of Glycosylated recombinant human granulocyte colony stimulating factor after high dose cytarabine-based induction chemotherapy for adult acute myeloid leukaemia. Bradstock KF, Matthews J, Young G, Lowenthal R, Baxter H, Arthur C, Brighton T, Cannell P,k Dunlop L, Durrant S, Enno A, Eliadis P, Gill D, Gillett A, Gottlieb D, Januszewicz H, Joshua D, Leahy M, Schwarer A, Taylor K and the Australian Leukaemia Study Group. *Leukemia*, provisionally accepted, 2001.

AUSTRALIAN AND NEW ZEALAND LYMPHOMA GROUP PUBLICATIONS

1. Australia and New Zealand non-Hodgkin's Lymphoma Cooperative Chemotherapy Study Group. Chairman IA Cooper.
A comparison of the use of Teniposide and Vincristine in combination chemotherapy for non-Hodgkin's lymphoma.
Cancer Treatment Reports 1982; 66 (1): 49-55.
2. Ding JC, Cooper IA, Firkin F, Matthews JP and Robertson TI.
Investigation of the additive potential of teniposide and vincristine in non-Hodgkin's lymphoma.
Cancer Treatment Reports 1986; 70 (8): 985-990.
3. Benson WJ, King JC and Cooper IA. (On behalf of the ANZ Lymphoma Group).
Abdominal CT and lymphography in the initial staging of non-Hodgkin's lymphoma.
Aust NZ J Med 1987; 17: 253-254.
4. Matthews JRD, Cooper IA, Matthews JP and Ding JC.
Failure of intensive chemotherapy in poor prognosis non-Hodgkin's lymphoma.
Aust NZ J Med 1992; 22: 123-128.
5. Cooper IA, Wolf MM, Robertson TI, Fox RM, Matthews JP, Firkin FC, Lowenthal RM, Ironside PNJ for the Australian and New Zealand Lymphoma Group.
Randomized Comparison of MACOP-B with CHOP in patients with intermediate-grade non-Hodgkin's Lymphoma. J Clin Oncol 1994; 12: 4.
6. Stone JM, Page PJ, Laidlaw CR, Cooper IA.
Selection of patients for randomised trials: A study based on the MACOP-B vs CHOP in NHL study. Aust NZ J Med 1994; 24: 536-540.
7. Morton J, Taylor K, Bunce I, Eliadis P, Rentoul A, Moore D, Kelly C, Wright S, Bashford J, Rodwell R, Rooney K, Mulligan S, Wolf M, Kirkin F, Dodds A, Parkin J, Lowenthal R, Kimber R, Frost T, Grigg A, Goldstein D, Stone J, Lee N.
High response rates with short infusional 2-chlorodeoxyadenosine in de novo and relapsed low grade lymphoma. Br J Haematol 1996; 95: 110-115.
8. Wolf M, Matthews JP, Stone J, Cooper IA, Robertson TE, Fox RM.
Long-term survival advantage of MACOP-B over CHOP in Intermediate-grade non-Hodgkin's lymphoma. Annals Oncol 1997; 8 (Supp.1): S71-S75.
9. Connors JM, Klimo P, Adams G, Burns BF, Cooper I, Meyer RM, O'Reilly SE, Pater J, Quirt I, Sadura A, Shustik C, Skillings J, Sutcliffe S, Verma S, Yoshida S, Zee B.
Treatment of advanced Hodgkin's disease with chemotherapy-comparison of MOPP/ABV hybrid regimen with alternating courses of MOPP and ABVD: a report from the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 1997; 15 (4): 1638-1645.

ALLG TRIALS COMPLETED IN 2000

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

HDNHL3 **Phase II study of DICE chemotherapy in lymphoma**

Report Date:	18 October 2000
Accrual target:	40
Date study opened:	1997
Date 1st patient enrolled:	17/7/97
Current total accrual:	40
Expected final accrual date:	-
Date study closed to accrual:	26/4/00
Main Trial Objectives:	Toxicities, Response Rates, PFS, OS
Trial Chairman:	Miles Prince
Number of sites known (by Trial Centre) to have Ethics Committee approval:	7
Number of sites with patients entered:	5
Trial Status:	Closed to accrual
Brief details of Serious/Unexpected Adverse Events experienced to date:	Nil
Publications:	HSANZ, Perth, July, 2000. Abstract, A Phase II Trial of Thalidomide in Patients with Multiple Myeloma (MM) followed by Intron-a® (Interferon Alfa-2b) Therapy. James J Biagi, H Miles Prince, Max Wolf, Henry Januszewicz, John Seymour, Andrew Grigg, Kate Lillie, Paul Mitchell, Department of Haematology, Peter MacCallum Cancer Institute, Melbourne, Victoria, Australia
Comments:	Plan to assess data in 2 nd quarter of 2001.

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

HDNHL1 Phase I/II Study of Irradiation with PBPCT in HD and NHL

Report Date:	17 October 2000
Accrual target:	30
Date study opened:	1997
Date 1st patient enrolled:	19/3/07
Current total accrual:	31
Expected final accrual date:	-
Date study closed to accrual:	17/12/99
Main Trial Objectives:	To evaluate the toxicity and efficacy of pre-and post-autograft radiotherapy to sites of bulk disease in relapsed lymphoma patients
Trial Chairman:	Andrew Wirth
Number of sites known (by Trial Centre) to have Ethics Committee approval:	6
Number of sites with patients entered:	5
Trial Status:	Closed to accrual, continued follow-up
Brief details of Serious/Unexpected Adverse Events experienced to date:	During pre-transplant RT: 2 patients with grade 3 haematological toxicity, no grade 4 During/after post-transplant RT: 4 patients with grade 3 haematological toxicity, no grade 4
Publications:	COSA 1999 Oral presentation accepted for International Congress of Radiation Oncology January 2001
Comments:	To be analysed in 2001.

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

LY1	Multicentre evaluation of NCI protocol 89-C-41 (with minor modifications) in Burkitt's or Burkitt-like NHL
Report Date:	17 October 2000
Accrual target:	60 (International)
Date study opened:	Oct 1995 (International), 1996 (ALLG)
Date 1st patient enrolled:	7/5/96
Current total accrual:	88 (International), 8 (ALLG)
Expected final accrual date:	-
Date study closed to accrual:	8/4/99
Main Trial Objectives:	Phase 2 study of intensive combination chemotherapy program for Burkitt's lymphoma
Trial Chairman:	Joe McKendrick
Number of sites known (by Trial Centre) to have Ethics Committee approval:	7
Number of sites with patients entered:	6
Trial Status:	Closed to accrual
Brief details of Serious/Unexpected Adverse Events experienced to date:	Nil
Publications:	ASCO 1999
Comments:	Study conducted in collaboration with UK Lymphoma Group.

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

NHL5 MACOP-B vs CHOP

Report Date:	18 October 2000
Accrual target:	300
Date study opened:	1986
Date 1st patient enrolled:	21/11/86
Current total accrual:	304
Expected final accrual date:	-
Date study closed to accrual:	27/6/91
Main Trial Objectives:	Randomised comparison of MACOP-B vs CHOP
Trial Chairman:	Ian Cooper (Max Wolf)
Number of sites known (by Trial Centre) to have Ethics Committee approval:	-
Number of sites with patients entered:	22
Trial Status:	Closed to accrual. Results published. Long-term follow-up to be published
Brief details of Serious/Unexpected Adverse Events experienced to date:	Nil
Publications:	J Clin Oncol; 12: 769-78, 1994 Aust NZ J of Med; 24: 536-540, 1994 Annals of Oncology; 8 (Suppl 1): S71-S75, 1997 Presented; VI International Conference on Malignant Lymphoma, Lugano, Switzerland, 5-8 June 1996; VII international Conference on Malignant Lymphoma, Lugano, Switzerland, 2-5 June 1999
Comments:	Nil

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

NHL-X3 **Bone marrow histology study**

Report Date:	10 October 2000
Accrual target:	250
Date study opened:	Feb 1999
Date 1st patient enrolled:	Feb 1999
Current total accrual:	200
Expected final accrual date:	-
Date study closed to accrual:	Dec 1999
Main Trial Objectives:	To study the incidence and prognostic significance of discordant marrow histology in DLCL
Trial Chairman:	Surender Juneja
Number of sites known (by Trial Centre) to have Ethics Committee approval:	N/A
Number of sites with patients entered:	Multicentre
Trial Status:	Closed
Brief details of Serious/Unexpected Adverse Events experienced to date:	N/A
Publications:	HSANZ 1999; ASH 1999

Comments:

For the analysis to be completed, the primary diagnosis needs to be reviewed by the histopathology review panel. We are awaiting this analysis for approximately 20 patients. Following this review we should be able to present the final analysis at the next ALLG meeting in Melbourne in May 2001. We should also be able to present the draft of the study manuscript for discussion.

LOW GRADE NHL / MYELOMA / CLL

NHLOW1 ASCT plus interferon in low grade NHL and mantle cell

Report Date:	19 October 2000
Accrual target:	50
Date study opened:	1995
Date 1st patient enrolled:	7/7/1995
Current total accrual:	60
Expected final accrual date:	-
Date study closed to accrual:	13/5/1999
Main Trial Objectives:	To examine the value of post-transplant Interferon in patients with low grade lymphoma
Trial Chairman:	Andrew Grigg
Number of sites known (by Trial Centre) to have Ethics Committee approval:	12
Number of sites with patients entered:	11
Trial Status:	Closed to accrual. Ongoing follow-up
Brief details of Serious/Unexpected Adverse Events experienced to date:	Nil
Publications:	Manuscript in preparation
Comments:	Good accrual to this study

ACUTE LEUKAEMIA

M7	A randomised phase III trial to evaluate the effect of high dose vs conventional dose cytarabine in consolidation therapy following intensive induction chemotherapy supported by lenograstim (fHu G-CSF) for adult acute myeloid leukaemia
Report Date:	6 October 2000
Accrual target:	200 evaluable patients in consolidation arm
Date study opened:	Sept 1995
Date 1st patient enrolled:	14/9/1995
Current total accrual:	206 in consolidation arm
Expected final accrual date:	-
Date study closed to accrual:	27/6/2000
Main Trial Objectives:	<ol style="list-style-type: none"> 1. To compare the leukaemia-free survival after consolidation therapy containing high dose cytarabine vs conventional cytarabine in AML patients induced into first remission with high dose cytarabine, idarubicin and etoposide. 2. To compare the duration of neutropenia after induction therapy in patients receiving lenograstim (G-CSF) vs no cytokine
Trial Chairmen:	Ken Bradstock / Graham Young / Ray Lowenthal
Number of sites known (by Trial Centre) to have Ethics Committee approval:	29
Number of sites with patients entered:	26
Trial Status:	Closed
Brief details of Serious/Unexpected Adverse Events experienced to date:	As previously reported. Await final analysis for complete details.
Publications:	Effects of Glycosylated Recombinant Human Granulocyte-Colony Stimulating Factor after High Dose Cytarabine-Based Induction Chemotherapy for Adult Acute Myeloid Leukaemia . (Submitted to Leukaemia, 2000). Kenneth Bradstock, Jane Matthews, Graham Young, Raymond Lowenthal, Chris Arthur, Timothy Brighton, Paul Cannell, Lindsay Dunlop, Simon Durrant, Arno Enno, Paul Eliadis, Devinder Gill, Ann Gillett, David Gottlieb, Henry Januszewicz, Douglas Joshua, Jerry Koutts, Michael Leahy, Anthony Schwarzer, Kerry Taylor, and the Australian Leukaemia Study Group.
Comments:	Expect to analyse results of consolidation trial in the fourth quarter of 2001.

ACUTE LEUKAEMIA

M8 **A phase II study of mitozantrone and intermediate-dose cytarabine in fit patients over 60 years of age with de novo acute myeloid leukaemia**

Report Date:	6 October 2000
Accrual target:	100
Date study opened:	November, 1995
Date 1st patient enrolled:	15/7/1996
Current total accrual:	45
Expected final accrual date:	-
Date study closed to accrual:	5/5/2000
Main Trial Objectives:	To evaluate complete response rate, remission duration and overall survival in patients over 60 years with de novo AML treated with intermediate dose cytarabine and mitozantrone
Trial Chairman:	Andrew Grigg
Number of sites known (by Trial Centre) to have Ethics Committee approval:	14
Number of sites with patients entered:	16
Trial Status:	Closed
Brief details of Serious/Unexpected Adverse Events experienced to date:	There were 4 instances of grade 4 toxicity, all in induction: 3 haematological, 1 cardiac. Besides alopecia, the grade 3 toxicities were limited to cutaneous (3 instances), N&V (4), Diarrhoea (2) and stomatitis (3) and occurred in both Induction and consolidation.
Publications:	Nil
Comments:	Formal evaluation due 5/2001. No update of patient survival to be done in 2000.

ALLG TRIALS IN PROGRESS

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

HD3 **Prospective study of limited chemotherapy and involved field radiotherapy for patients with clinical stage I-II Hodgkin's Disease**

Report Date:	18 October 2000
Accrual target:	150
Date study opened:	1999
Date 1st patient enrolled:	10/5/1999
Current total accrual:	77
Expected final accrual date:	March, 2001
Date study closed to accrual:	-
Main Trial Objectives:	To estimate 3 and 5 year progression-free survival after 3 (4) cycles of ABVD and IFRT in patients with early stage HD
Trial Chairman:	Andrew Wirth
Number of sites known (by Trial Centre) to have Ethics Committee approval:	31
Number of sites with patients entered:	24
Trial Status:	Open to accrual
Brief details of Serious/Unexpected Adverse Events experienced to date:	Eight Serious Adverse Events have been reported in this trial since it began accrual in May 1999. Of the eight, four of the events were believed to be related to the study drugs, they included febrile neutropenia, myalgia, postural hypotension and pneumonitis.
Publications:	Nil
Comments:	Consideration is being given to raising the accrual target to 150.

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

TROG 99.04 ALLG LY2 **A non-randomised prospective study of Osteolymphoma**

Report Date: 4 October 2000

Accrual target: 70

Date study opened: September, 1999

Date 1st patient enrolled: N/A

Current total accrual: (2)

Expected final accrual date: 2010

Date study closed to accrual: -

Main Trial Objectives: To optimise overall survival, determine prognostic factors, avoid pathological fractures and study natural history.

Trial Chairman: David Christie

Number of sites known (by Trial Centre) to have Ethics Committee approval: 9

Number of sites with patients entered: (2)

Trial Status: Open to accrual

Brief details of Serious/Unexpected Adverse Events experienced to date: Nil

Publications: Follows on from retrospective survey (Christie et al, ANZJMed, 1999)

Comments:

Two patients awaiting registration subject to eligibility checks.
Funding approved from Wesley Research Institute - \$300 per patient.

INTERMEDIATE & HIGH GRADE NHL/ HODGKIN'S DISEASE

NHL8 **Trial to evaluate early HDCT and ABMT as part of planned initial therapy for poor risk intermediate grade NHL**

Report Date:	18 October 2000
Accrual target:	500 Internationally
Date study opened:	1992
Date 1st patient enrolled:	4 December 1992 (ALLG)
Current total accrual:	425 October 1999 (International) 48 (ALLG)
Expected final accrual date:	2001
Date study closed to accrual:	-
Main Trial Objectives:	To compare elective auto transplantation in first remission with standard chemotherapy in patients with poor prognosis intermediate grade NHL.
Trial Chairman:	Joe McKendrick
Number of sites known (by Trial Centre) to have Ethics Committee approval:	11
Number of sites with patients entered:	11
Trial Status:	Open to accrual
Brief details of Serious/Unexpected Adverse Events experienced to date:	Nil
Publications:	Nil
Comments:	Study being conducted in collaboration with UK Lymphoma Group.

LOW GRADE NHL / MYELOMA / CLL

CLL2

International phase 3 trial of primary therapy for B-Cell chronic lymphocytic leukaemia.

Report Date:	6 October 2000
Accrual target:	500 International
Date study opened:	November 1998 (Aust) 15 November 1997 (International)
Date 1st patient enrolled:	26 March, 1999 (Aust) 25 November, 1999 (International)
Current total accrual:	30 (Aust) 93 (International)
Expected final accrual date:	31 March 2003 (International)
Date study closed to accrual:	-
Main Trial Objectives:	To evaluate the efficacy and toxicity of chlorambucil, fludarabine and cladribine, as primary treatment of previously untreated patients with symptomatic B-cell CLL.
Trial Chairman:	Stephen Mulligan
Number of sites known (by Trial Centre) to have Ethics Committee approval:	16
Number of sites with patients entered:	14
Trial Status:	Open to accrual
Brief details of Serious/Unexpected Adverse Events experienced to date:	30 patients have been entered in Australia of which 6 have been randomised a second time according to protocol. SAE's include severe cutaneous reaction to one of the protocol drugs.
Publications:	Nil
Comments:	International collaborative trial with Scandinavian and British investigators.

LOW GRADE NHL / MYELOMA / CLL

NHLOW4 CHOP ± MabThera in relapsed follicular NHL

Report Date:	19 October 2000
Accrual target:	152 (Internationally) 100 (ALLG)
Date study opened:	1999
Date 1st patient enrolled:	1 February 1999
Current total accrual:	71 (International) 21 (ALLG)
Expected final accrual date:	2001
Date study closed to accrual:	-
Main Trial Objectives:	Randomised study of CHOP +/- MabThera. The objectives are to determine the effect of addition of MabThera to CHOP in relapsed low-grade NHL on response and to determine the effect of maintenance MabThera on progression-free survival.
Trial Chairman:	Max Wolf
Number of sites known (by Trial Centre) to have Ethics Committee approval:	39
Number of sites with patients entered:	12
Trial Status:	Open to accrual. Protocol recently amended.
Brief details of Serious/Unexpected Adverse Events experienced to date:	International summary of SAE's received by EORTC Safety Desk by September 2000 indicates that there have been 14 events comprising 17 conditions (3 events involved 2 conditions each). One patient has died, 1 had a life threatening event, 11 were hospitalised and 1 experienced a disability. Six events were coded as definitely or probably related to treatment consisting of one each of: infection, allergy, febrile neutropenia, hyperglycemia, delayed neutropenia and hypocalcemia.
Publications:	Nil
Comments:	Study conducted in collaboration with EORTC and 6 other cooperative groups internationally. Poor accrual internationally. Recent amendment (EORTC Amendment 4) improves the eligibility criteria and hopefully will result in an improved accrual.

LOW GRADE NHL / MYELOMA / CLL

**TROG99.03
ALLG -
NHLLOW5** **A randomised multicentre trial of involved field radiotherapy versus involved field radiotherapy plus chemotherapy for stage I-II low grade follicular lymphoma**

Report Date: 19 October 2000

Accrual target: 200

Date study opened: August 1999

Date 1st patient enrolled: 14 February 2000

Current total accrual: 2

Expected final accrual date: December 2005

Date study closed to accrual: -

Main Trial Objectives: Primary Objective:
 - Study effect of CVP x 6 on progression-free survival in Stage I-II low grade FL treated with IFRT
 Secondary Endpoints:
 - t(14;18): Value of “molecular remission”
 - Overall survival
 - Toxicity
 - Patterns of failure
 - Transformation

Trial Chairman: Michael MacManus
John Seymour

Number of sites known (by Trial Centre) to have Ethics Committee approval: 15

Number of sites with patients entered: 1

Trial Status: Open to accrual

Brief details of Serious/Unexpected Adverse Events experienced to date: Nil

Publications: Nil

Comments:
Early accrual slow.

MYELOPROLIFERATIVE DISEASE / MYELODYSPLASIA

YNK01**YNK01 / Intron study in CML**

Report Date:	October 2000
Accrual target:	64 (evaluable in 1A/1B)
Date study opened:	December 1997
Date 1st patient enrolled:	December 1997
Current total accrual:	2x32 EVA
Expected final accrual date:	Uncertain
Date study closed to accrual:	-
Main Trial Objectives:	To examine efficacy of YNK01 and Intron-A in de novo chronic myeloid leukaemia
Trial Chairman:	Kerry Taylor
Number of sites known (by Trial Centre) to have Ethics Committee approval:	12
Number of sites with patients entered:	12
Trial Status:	Trial was conducted on two consecutive cohorts: 1A - intermittent YNK01 – reached accrual 1B - continuing accrual
Brief details of Serious/Unexpected Adverse Events experienced to date:	Toxicity has included aesthenia, gastrointestinal intolerance, cytopenias and hepatitis (see ASH 2000)
Publications:	Phase II study of Interferon alpha + Oral Cytarabine in Treatment of Newly Diagnosed CML – accepted for oral presentation ASH 2000.
Comments:	Accrual to 1B has been slow due to competing STI studies.

ACUTE LEUKAEMIA

APML3

A phase 2 trial in patients with acute promyelocytic leukaemia to evaluate the effects of:

1. All-trans retinoic acid combined with intensive idarubicin during induction and consolidation;
2. Subsequent intermittent all-trans retinoic acid; and,
3. Molecular monitoring for evidence of minimal residual leukaemia and for evidence of incipient relapse

Report Date: 6 October 2000

Accrual target: 100

Date study opened: June 1997

Date 1st patient enrolled: 19 August 1997

Current total accrual: 59

Expected final accrual date: Mid 2002

Date study closed to accrual: -

Main Trial Objectives: To maximise the complete remission rate by combining all-trans retinoic acid (ATRA) with intensive idarubicin chemotherapy, to minimise relapse rate by employing a second course of idarubicin followed by intermittent ATRA for eradication of minimal residual leukaemia, and to maximise overall survival through an intensive program of molecular monitoring for the detection of incipient relapse combined with an aggressive therapeutic intervention strategy aimed at eradication of low levels of recurrent leukaemia.

Trial Chairmen: Harry Iland / Jim Wiley / Frank Firkin

Number of sites known (by Trial Centre) to have Ethics Committee approval: 26

Number of sites with patients entered: 23

Trial Status: Open to accrual

Brief details of Serious/Unexpected Adverse Events experienced to date:

- First 42 patients reviewed in May 2000
- Four early deaths during induction with Idarubicin #1
- One death during consolidation after Idarubicin #2
- Grade 3-4 cardiotoxicity in 5 patients (4 after Idarubicin #1, 1 after Idarubicin #2)
- Two patients withdrawn from study (1 resistant disease, 1 cardiotoxicity)

ACUTE LEUKAEMIA

**APML3
(Contd)**

A phase 2 trial in patients with acute promyelocytic leukaemia to evaluate the effects of:

- 1. All-trans retinoic acid combined with intensive idarubicin during induction and consolidation;**
- 2. Subsequent intermittent all-trans retinoic acid; and,**
- 3. Molecular monitoring for evidence of minimal residual leukaemia and for evidence of incipient relapse**

Publications:

Nil but presented in part at MRD Symposium at HSANZ Annual Meeting, Perth 2000

Comments:

Maintenance program added for ALLG meeting in May 2000 because of higher than expected incidence of molecular relapse.

ACUTE LEUKAEMIA

ALL2 - LALA94 **A multicentre trial of induction and post-remission therapy of adult acute lymphoblastic leukaemia**

Report Date: 6 October 2000

Accrual target: 1000 (worldwide, induction)

Date study opened: June 1994 (November 1995 in Australia)

Date 1st patient enrolled: June 1994 (27 November 1995 in Australia)

Current total accrual: 865 (65 ALLG)

Expected final accrual date: Mid July 2001

Date study closed to accrual: -

Main Trial Objectives: This is a complex trial examining several risk-stratified questions in induction and consolidation therapy for adult ALL. In the induction phase, there was a comparison of the anthracyclines Daunorubicin and Idarubicin. Post-induction, in standard risk patients, there is a comparison of two chemotherapy regimens for consolidation therapy. In high-risk patients, a comparison of maintenance chemotherapy with early autologous stem cell transplantation is being carried out in patients lacking a histocompatible sibling donor.

Trial Chairmen: Denis Fiere (France) / Ken Bradstock

Number of sites known (by Trial Centre) to have Ethics Committee approval: 8

Number of sites with patients entered: 8

Trial Status: Open for accrual. Induction anthracycline randomisation Closed.

Brief details of Serious/Unexpected Adverse Events experienced to date: No unexpected serious toxicities identified at last review meeting April 1999.

Publications: Nil

Comments: International collaborative study with French Adult ALL Group.

BONE MARROW TRANSPLANTATION

Mini allograft study in chronic myeloid leukaemia and myeloma

Report Date:	26 October 2000
Accrual target:	40
Date study opened:	January 1999
Date 1st patient enrolled:	18 August 1999
Current total accrual:	23
Expected final accrual date:	December 2001
Date study closed to accrual:	-
Main Trial Objectives:	To assess the timing and characteristics of donor engraftment in patients receiving T-cell depleted peripheral blood stem cell allografts after non-myeloablative conditioning therapy.
Trial Chairmen:	Tim Hughes / Peter Bardy
Number of sites known (by Trial Centre) to have Ethics Committee approval:	7
Number of sites with patients entered:	5
Trial Status:	Currently accruing
Brief details of Serious/Unexpected Adverse events experienced to date:	Unexpected high rejection rate in myeloma and high relapse rate in CML.
Publications:	EBMT 2000 oral presentation ASH 2000 poster
Comments:	Study modified to increase T cell dose and to reduce intensity of conditioning therapy.

BONE MARROW TRANSPLANTATION

Pamidronate post allogeneic bone marrow transplantation

Report Date:	25 October 2000
Accrual target:	100
Date study opened:	March 1999
Date 1st patient enrolled:	March 1999
Current total accrual:	65
Expected final accrual date:	June 2001
Date study closed to accrual:	-
Main Trial Objectives:	To assess whether pamidronate prevents loss of BM density after allo BMT
Trial Chairmen:	Andrew Grigg
Number of sites known (by Trial Centre) to have Ethics Committee approval:	5
Number of sites with patients entered:	4
Trial Status:	Ongoing, accruing well
Brief details of Serious/Unexpected Adverse events experienced to date:	Hypocalcaemia; prevented by prior Ca ² + supplementation
Publications:	Nil, too early. No analyses yet.
Comments:	Good study

BONE MARROW TRANSPLANTATION

MabThera post autograft for mantle cell lymphoma

Report Date:	25 October 2000
Accrual target:	12 (initially)
Date study opened:	May 1999
Date 1st patient enrolled:	June 1999
Current total accrual:	8
Expected final accrual date:	August 2001
Date study closed to accrual:	-
Main Trial Objectives:	To assess the tolerability of MabThera post autograft; molecular analysis as a secondary end-point
Trial Chairmen:	Andrew Grigg
Number of sites known (by Trial Centre) to have Ethics Committee approval:	8
Number of sites with patients entered:	5
Trial Status:	Ongoing
Brief details of Serious/Unexpected Adverse events experienced to date:	None
Publications:	Nil
Comments:	Ongoing trial; limited molecular data

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