Mantle cell

430 PROGNOSTIC IMPACT OF CLINICAL AND TUMOR ASSOCIATED VARIABLES IN A POPULATION-BASED COHORT OF MANTLE CELL LYMPHOMAS IN THE STOCKHOLM REGION BETWEEN 1998-2010

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Introduction: Mantle cell lymphoma (MCL) constitutes 3-10% of non-Hodgkin lymphomas. It predominantly affects middle-aged to elderly men and is often advanced at diagnosis. The median survival is 3-5 years and has improved with new therapeutic regimens. The MCL International Prognostic Index, MIPI, has been proven useful for predicting survival in patients with advanced MCL included in clinical trials. The value of MIPI in unselected clinical cohorts remains to be investigated.

Patients and Methods: All MCL diagnosed and confirmed with IHC and/or FISH between January 1998 and June 2010 (n=186) in the Stockholm region, were included in a population based, retrospective analysis. The following variables evaluated at the time of diagnosis were analyzed with respect to overall survival: age, sex, Ann Arbor stage, ECOG>2, B-symptoms, Hb, LDH, albumin leukocytosis ($>10*10^9$), splenomegaly, bone marrow involvement, proliferation, blastoid morphology, p53 positivity (>20% of cells) and nuclear SOX11 expression.

Results: The male:female ratio was 2 and the median age at diagnosis 68,8 years (range 36,2-89,9); 67,4 in males and 72,1 in females, respectively. Median survival time was 3,4 years in the whole cohort and 2,9 years when excluding the 41 patients receiving high dose chemotherapy and ASCT. In univariate analysis the following clinical variables were significantly negatively correlated to overall survival in the whole cohort: age >65 years, bone marrow involvement, B symptoms, splenomegaly, ECOG>2, low albumin, high WBC, lymphocytosis $> 5x10^9$/L ($p< 0,001$) and high LDH ($p<0,05$). High tumor cell proliferation, blastoid morphology and p53 positivity was also negatively correlated to overall survival. If excluding patients receiving ASCT, LPK and lymphocytis were no longer significant, while the remaining variables were still significantly ($p<0,05$) associated to dismal prognosis. In contrast, ten patients showed clinically indolent MCL not requiring treatment, with a median follow up of 2,8 years (range 1 – 9,6 years).

Conclusions: Compared to data of previous reports based on clinical studies of advanced MCL, our patients were at an older age when diagnosed, which may contribute to the shorter overall survival. Certain well-established prognostic variables seem to loose significance outside study populations. The results of multivariate analyses and further characteristics of the patients with indolent disease will be presented.

431 SERUM FREE LIGHT CHAIN RATIO – A POTENTIAL BIOMARKER FOR MANTLE CELL LYMPHOMA

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Introduction: Serum kappa and lambda free light chain (SFLC) levels and the K/L free light chain ratio are standard measures in monoclonal plasma cell dyscrasias – an abnormal SFLC ratio indicating monoclonality and a worse prognosis. A proportion of Non Hodgkin's Lymphoma (NHL) patients also demonstrate abnormal SFLC ratios, the significance of which is unclear. Mantle cell lymphoma (MCL) represents 5% of NHL and is associated with a poor overall patient survival. Previous studies have shown a high frequency of abnormal SFLC ratios (36-70%) in MCL. We hypothesised that the Freelite immunoassay (Binding Site, UK) may be beneficial in MCL clinical monitoring and patient management.

Methods: Analysis of frozen sera from 31 MCL patients was undertaken in a two stage process (total: 188 samples). An initial 11 MCL patients, presenting to Derriford Haematology service, were screened for serum free light chain abnormalities. Thereafter, 20 relapsed/ refractory MCL patients, enrolled in a phase II clinical trial of single agent lenalidomide (EuDRACT No 2007-005472-13) provided a more uniformly treated MCL patient population for subsequent analysis. All patients had a sample from trial entry analysed alongside a variable number of follow up samples at pre-set post chemotherapy cycle time points, to a maximum of 1 year post trial entry.

Results: At trial entry 35% patients (7/20) had abnormal SFLC ratios, 3 patients also had concomitant elevated total free light chain level (i.e. = SFLC kappa + SFLC lambda > 50mg/L). 5 of the 7 patients with an abnormal SFLC ratio at trial entry had serial samples analysed. These showed a strong correlation between disease improvement (reduction in lymph node size and resolution of symptoms) and SFLC ratio normalisation. 2 of the 7 patients had no serial samples analysed due to death or disease progression. Of note, for patients with an elevated SFLC ratio at trial entry a rise in the SFLC ratio of >35% (using ratio at presentation as 0%) correlated with disease progression. In addition a SFLC ratio of >2x upper limit of normal at trial entry correlated with aggressive disease (significant disease progression or death within 2 months).

Conclusions: Our results are the first to show a clear clinical correlation between SFLC ratios and MCL disease behaviour. We suggest that these markers may be useful in managing patients with MCL in the future.

432 CD23 EXPRESSION IN MANTLE CELL LYMPHOMA (MCL): AN ANALYSIS OF BIOLOGIC CORRELATIONS AND CLINICAL OUTCOMES

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Background: MCL is typically: CD5+CD20+CD10−CD23−FMC7+cyclinD1+, with a monotypic surface immunoglobulin light chain. A minority of MCL express CD23. MCL is an aggressive disease with poor outcomes, but some cases display indolent behaviour. Previous reports showed that extranodal presentation, hypermutated IGVH, absence of SOX11 expression are qualities of this latter type. Some studies have described a better outcome of MCL with CD23 expression, but others found no prognostic value of CD23 expression. Aim of our study was to investigate CD23 expression in MCL and correlate this expression with clinical parameters.

Methods: We retrospectively investigated CD23 expression by flow cytometry in bone marrow (BM) and peripheral blood (PB) samples in 52 patients (pts) with MCL, and correlated CD23 expression with biologic and clinical parameters. Pts median age was 64 years (range 33-83), male/female ratio 37/15, 45 pts (87%) had stage III-IV, 41 (79%) BM and 22 (43%) PB involvement, 8 (15%) splenic involvement, 25 (48%) B symptoms and 21 (41%) a MIPI score ≥ 5. In 44 (85%) pts Ki67 was >= 20, in 18 (35%) LDH and in 44 (85%) β2μglobulin was high. CD23 was positive in 12 (23%) pts. No statistically significant different features were observed in the two groups, CD23 pos and neg. Forty-four (85%) pts received CHOP like chemotherapy, 8 (15%) HyperCVAD.

Results: CD23 expression was present in 12 (23%) pts; 9 (78%) CD23+ and 37 (92%) CD23- pts were responsive to treatment (p: n.s.): 3 (22%) and 10 (25%) achieved Complete Remission (CR) and 6(55%) and 27 (67%) Partial Remission, respectively. Three (22%) CD23+ and 3 (8%) CD23- pts had progressive disease. At a median follow-up of 30 months (range 2-120) Overall Survival (OS) is 58% and Progression Free Survival (PFS) 30%. Parameters that had an impact on the overall Response Rate (ORR) were: III-IV stage, β2μglobulin, BM involvement. No statistically significant differences between the two groups were observed for ORR, OS, PFS and prognostic parameters.

Conclusions: Some studies have reported a better prognosis with CD23 expression in MCL, but the incidence of CD23+ MCL is not well known and the correlation between CD23 expression and clinical outcome is not clear. In accordance with others papers, in our study no statistically significant differences in terms of ORR, OS and PFS were observed between the two groups CD23+ and CD23- MCL. Further biological studies are needed to explain the prognostic value of CD23 expression in MCL and establish whether CD23+ MCL is a distinct clinico- pathologic entity.

433 FIRST LINE TREATMENT WITH ANTHRACYCLINE-BASED REGIMEN WITH OR WITHOUT RITUXIMAB IN PATIENTS WITH MANTLE CELL LYMPHOMA (MCL)

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Background: MCL represent a distinct group of NHL, with an aggressive clinical course, poor prognosis and a median survival 3-4 years.

Methods: In this study we retrospectively analysed the clinical outcome of patients with MCL, who received CHOP like regimen with or without rituximab in our centre. Patients characteristics are showed in Table 1.

Characteristics	No
Patients	43
Age: median	63,
range	40-83
Gender: male / female	35 / 8
Ann Arbor stage: I-II / III-IV	7 /36
IPI score low/int-lowint-high / high	5 /14, 14 /10
MIPI score: low/in high	8 / 19, 16
B-symptoms	9
Bone marrow	29
Treatment: CHOP / R-CHOP/other	14/20,/9

Results: The median follow up was 28 months (5-125 months). From 43 patients, 20 died and 17 relapsed. The treatment was well tolerated and none patient died, due to treatment toxicity. The estimated median OS was 46 months and the estimated median PFS was 36 months for all patients. The IPI score seems to be statistical significant for the disease progression and survival. Patients with low or intermediate IPI score, had an estimated median OS 48 months vs 28 months for patients with high IPI score (p=0,0034) and PFS was 36 months vs 7 months respectively (p=0,034). In this group of pts MIPI score, had marginal statistical significant in OS. Patients with low or intermediate MIPI score had median OS 49 vs 36 months for patients with high MIPI score (p=0,1), and PFS 36 vs 18 months respectively. The stage of disease, the bone marrow involvement and the B-symptoms seems to have no impact in OS. The addition of rituximab as frontline therapy, had no statistical significant in OS and PFS. The median OS in R-CHOP group of patients, was 64 vs 46 months for patients who received CHOP(p=0,35) and median PFS 36 vs 34 months respectively (p=0,71).

Conclusion: The results of our study confirm the bad prognosis of MCL with conventional CHOP like regimen. The only parameters which influence significantly the OS and the PFS of these patients is the IPI score. The addition of rituximab has no benefit in OS and consequently more intensives therapies should be used in patients with MCL.

434 R-GIFOX (RITUXIMAB, GEMCITABINE, IFOSFAMIDE, OXALIPLATIN) PLUS RITUXIMAB MAINTENANCE AS FIRST-LINE STRATEGY IN CLASSICAL MANTLE CELL LYMPHOMA

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Background: The incorporation of new agents in upfront strategies of mantle-cell lymphoma (MCL) is a present challenge to investigators. Benefit gained by including an anthracycline into conventional chemotherapy is not entirely clear, and there is no evidence that currently available aggressive programs are curative or prolong overall survival. We evaluated as 1st-line treatment a dose-dense combination of the agents rituximab (R), gemcitabine (G), ifosfamide (Ifo) and oxaliplatin (Ox) (R-GIFOX), all accounted of good single-agent and synergistic activity in MCL.

Methods: 6 R-GIFOX courses were given at 2-week intervals and followed by maintenance with R all 2-months. No transplant procedure was programmed, but a back-up collection of peripheral CD34+ cells was provided in eligible pts. Schedule: G 1200 mg/m^2 D1, Ox 120 mg/m^2 D2 and Ifo 5 g/m^2 D2, as a 24h infusion in pts ≤65 yrs, or fractionated over DD 2, 3 and 4 in pts >65, G-CSF 5 mcg/kg/d DD 7-11. At recycling, treatment was delayed until ANC >1000/μL and Plt >75000/μL with doses reduced according to nadir. A strict monitoring of Cl_{cr} was required and Ifo dose reduced according to Kintzel (*Cancer Treat Rev*, 1995, 21(1):33-64).

Results: Sixteen newly-diagnosed MCL pts (M/F=10/6; median age 66 yrs, r 43-78)[blastoid cytologic variant (n=2)] were prospectively accrued in a pilot study from January 2005 to June 2007 [stage IV: 88%; E-site >1: 68%; abn LDH: 56%]. Overall 89 cycles were delivered; all but 3 pts, aged >65 yrs, received the whole program. Interruptions were due to grade 2 and 3 encephalopathy (4th course) and grade 3 tachyarrhythmia (3rd course), but pts went up to 6 cycles, after omitting Ifo. Grade 4 thrombocytopenia occurred in 7 pts (43%), grade 4 anemia and grade 3 infection in 31% and 37%, respectively. No patient died from acute toxicity. The ORR was 100% (95% CI: 77-100), with 2 PR and 14 CR (88%; 95% CI: 63-98). The 5-year Progression-Free Survival was 56% without a plateau in the curve and any clear difference between pts younger or older than 65 yrs.

Conclusions: R-GIFOX appears highly effective and well-tolerated in MCL patients, so deserving larger prospective studies. It may represent an alternative to anthracycline-based chemotherapy and an attractive substitute for current more toxic intensified programs including high-dose cytarabine and cisplatin (R-Hyper-CVAD/hdMC, R-DHAP) especially in pts older than 65 yrs, for whom these regimens are not recommended.

435 EFFICACY AND SAFETY OF A SEQUENTIAL TREATMENT CONTAINING ARA-C AND HIGH DOSE ANTHRACYCLIN/MELPHALAN AS MYELOABLATIVE REGIMEN FOR PATIENTS WITH MANTLE CELL LYMPHOMA: REPORTS OF A PHASE II STUDY

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Introduction: Mantle cell lymphoma (MCL) still maintains a poor long term prognosis and the use of Rituximab have not been changed the outcome like as in other lymphomas. However the use of induction treatment containing high-dose cytarabine (HDARA-C) followed by a consolidation with myeloablative regimens resulted in a significant prolongation of EFS.

Method: To evaluate the safety and efficacy of a sequential treatment containing HDARA-C and autologous transplantation, we treated on an intention to treat basis, all newly MCL diagnosed pts with 4 cycles of R-CHOP-like regimen followed by high-dose R-Cyclophosphamide at 4g/sqm to collect peripheral blood stem cells, 2 cycles of HDARA-C-based regimen (R-ESHAP) and then transplant using high dose of R-Melphalan (180mg/mq) in combination with Idarubicin (15mg/mq x 3 days) or Novantrone (60mg/mq x 1day).

Results: From May 1997 to August 2009, 27 pts were treated and all of them were able to conclude the program. Median age was 55yrs (range 37-67), male 78%, stage IV 70%, MIPI high risk 12%. After induction, overall response rate was 88% with 19 CR/CRu (70%). After transplantation overall response rate and CR rate were 96% and 89% respectively. Toxicity of conditioning regimen consisted mainly in grade 3-4 mucositis (37%); all pts received more than 2x10(6) CD34+ cells (range 2.2-11.5) and 4 pts experienced a late engraftment. With a median follow-up of 44 months (range 21-109), median PFS is 20 months (range 1-40) with 11 pts (41%) still in CR. Seven patients died for PD, 2 patients for TRM after an allotransplant and one patient in CR for cardiac failure 7 yrs after transplantation; overall survival observed is 63%.

Conclusions: Our experience confirms that a sequential treatment approach containing an induction with HDARA-C and a consolidation with high-dose chemotherapy is a valid strategy to induce high-response rate and a long-term disease control.

436 THERAPY WITH BORTEZOMIB + LENALIDOMIDE IS TOLERABLE IN PATIENTS (PTS) WITH RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA (MCL): INTERIM RESULTS OF CALGB 50501

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Introduction/Background: Although initial treatment response, alone or with stem cell transplant (SCT) is common in MCL pts, virtually all pts develop relapse/recurrent disease. Single agent bortezomib activity in relapsed/refractory MCL pts has been demonstrated, with 33-50% response rates, and 9-10 months (mos) median remission duration. Thalidomide + rituximab has also been examined in MCL pts, with 81% response rate and 20 mos progression-free survival. Single agent lenalidomide in relapsed/refractory MCL pts has demonstrated a 41% response rate, but significant grade (gr) 3/4 myelosuppression.

Patients and Methods: CALGB 50501 is an ongoing phase II study of bortezomib + lenalidomide for relapsed/refractory MCL pts. Eligibility criteria include: histologically documented MCL (CD5+, CD 23-, cyclin D1+); measurable disease; prior therapy with >1 regimen including autologous, but not allogeneic, SCT; no prior radioimmunotherapy; PS 0-2; no peripheral neuropathy >gr 3. Induction therapy is lenalidomide (20 mg po qd, days (d) 1-14) plus bortezomib (1.3 mg/m2 IV, d1, 4, 8, 11), every 21d for 8 cycles. Pts with responsive disease (CR/PR) at 6 mos go onto maintenance with lenalidomide (15 mg po qd, d1-14) and bortezomib (1.3 mg/m2 IV, d1, 8), which is continued until disease progression. Primary endpoint is overall response rate (CR+PR); secondary endpoints are time to progression; disease-free and overall survival; correlative science studies of changes in NK/activated T-cells and plasma cytokines with response. Accrual goal is 54 (49 eligible/evaluable) pts. The study was activated in 11/07, and modified in 9/09 to have separate dose reductions for each agent (e.g., myelosuppression, lenalidomide; neuropathy, bortezomib).

Results: As of 1/11/11, 48 pts have been accrued, with interim toxicity data available for 44 pts as follows:

	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)
Anemia	25	5	0
Leukopenia	23	7	0
Neutropenia	23	11	5
Thrombocytopenia	23	14	18
Hypotension	9	9	0
Fatigue / asthenia	18	20	0

Rash	9	2	0
Anorexia	14	5	0
Diarrhea	9	9	2
Nausea	16	2	0
Febrile neutropenia	0	2	0
Infection, clinically documented	0	5	0
Sensory neuropathy	43	5	0
Motor neuropathy	7	11	0
Dyspnea	5	11	0
Thrombosis/embolism	0	5	0

Conclusions: These interim data suggest that bortezomib + lenalidomide has acceptable toxicity in relapsed/refractory MCL pts. Interim efficacy data have met the threshold for completing pt accrual (6/2011).

437 THE ADDITION OF RITUXIMAB TO WEEKLY INFUSION OF BORTEZOMIB IS SAFE AND EFFECTIVE IN RELAPSED/ REFRACTORY INDOLENT NON FOLLICULAR AND MANTLE CELL LYMPHOMA: LONG TERM RESULTS OF PHASE II TRIAL BRIL06 OF ITALIAN LYMPHOMA FOUNDATION (FIL)

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Background: Bortezomib (B) is effective in relapsed mantle cell lymphoma (MCL) and is synergistic with Rituximab (R) to enhance apoptosis and NFkB depletion. On these basis, the FIL conducted a phase II multicenter study aimed to evaluate safety and efficacy of B in association with R in relapsed/refractory non-follicular Lymphoma (Linfocytic, LL and Marginal Zone, MZL) and MCL.

Patients and Methods: Inclusion criteria were: 18-75 years, relapsed/refractory LL, MZL, MCL after 1-4 lines. Treatment schedule was: one course of 1.6 mg/sqm B in combination with standard R on days 1,8,15,22 followed by two courses of weekly B alone; in responsive patients, three further courses with the same schedule were planned.

Results: From 2006 to 2008, 55 patients were enrolled and 6 were excluded at central histological revision. Clinical characteristics were: median age 68 (50-74); 16 LL, 8 MZL, 25 MCL; 42 stage III/IV; 33 bone marrow involvement. Thirty-eight patients were at third or fourth relapses, 34 R-pretreated; 21 had refractory disease. Overall Response Rate (ORR) was 53% (complete response 26.5%); no response was 43% and 4% off therapy. ORRs by clinical subgroup were: LL 37%, MZL 50%, MCL 64%; R-pretreated 62%, R-naïve 33%; relapsed 64% and refractory 38%. With a median follow-up of 26 months, median Overall Survival was not reached and median Progression Free Survival (PFS) was 9.9 months (95%CI:4.8-18.3). Median PFS by histology was: 4.8 (95%CI:4.1-8.9) for LL, 18.3 (5.3-29.9) for MCL and 9.9 months (2.4-not reached) for MZL. Thirty patients completed the treatment and 233 courses were delivered (median: 4.7 courses/patient); 19 patients did not because of no response in 13, adverse events in five with only one toxic death due to interstitial pneumonia). Grade 3-4 CTC haematological toxicity was rare: neutropenia in 5% and thrombocytopenia in <2% of all courses. Grade 3-4 CTC non-hematological toxicities were: neurotoxicity grade III in four (all completely recovered); infections in eight patients: viral reactivation, bacterial pneumonia and micosis.

Conclusions: Weekly infusion of B in combination with R is effective and safe in relapsed/refractory indolent and MCL, also in R-pretreated patients. Data demonstrated that this schedule is effective mainly in MZL and MCL.

438 EFFICACY AND SAFETY OF CONVENTIONAL-DOSE LENALIDOMIDE FOLLOWED BY LOW-DOSE MAINTENANCE LENALIDOMIDE FOR RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA (MCL): RESULTS FROM A UK PHASE II STUDY

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Introduction: Lenalidomide at a long-term fixed dose of 25mg daily has proven clinical efficacy in relapsed/refractory MCL, producing response rates of 53% and 43% in the NHL-002 and NHL-003 trials respectively. We present data from a phase II study investigating a novel treatment strategy for this disease that incorporates a period of conventional-dose lenalidomide (25mg) followed by low-dose maintenance lenalidomide (15mg) in responding patients.

Methods: Patients with relapsed/refractory MCL and measurable disease after at least 2 prior therapies were eligible. Patients initially received lenalidomide at a ''treatment dose'' of 25mg daily on days 1-21 of a 28-day cycle for up to 6 cycles. Responding patients (those who achieved complete response (CR), complete response unconfirmed (CRu), partial response (PR) or stable disease (SD)) continued lenalidomide at a ''maintenance dose'' of 15mg daily on days 1-21 of a 28-day cycle until disease progression, unacceptable toxicity, or consent withdrawal.

Results: 26 patients were enrolled with a median age of 66 years (range 45-81) and median disease duration of 3.9 years (range 0.3-12.9). The median number of prior therapies was 3 (range 2-8), including bortezomib in 8 patients (31%), stem cell transplantation in 6 patients (23%), and thalidomide in 2 patients (8%). One patient achieved CR and 8 patients achieved PR to give an overall response rate of 35% with an estimated median response duration of 8.6 months (range 2.0-20.4). Five additional patients (19%) achieved SD with an estimated median response duration of 7.3 months (range 0.9-10.3). One patient (4%) progressed during therapy. The remaining 11 patients (42%) withdrew after <2 complete cycles of lenalidomide due to progressive disease (n=5), adverse events (n=4) or consent withdrawal (n=2). 11 patients received maintenance lenalidomide, of which 4 remain on drug. Estimated median progression-free survival for the entire study population is 3.9 months, and for the maintenance cohort is 14.6 months. The most common grade 3-4 toxicities were neutropenia (36%) and thrombocytopenia (36%). Both haematological and non-haematological toxicities were less frequent and severe on maintenance-dose than treatment-dose lenalidomide.

Conclusions: Our study confirms the efficacy and safety of single-agent lenalidomide in relapsed/refractory MCL. Moreover, continuing lenalidomide at a lower maintenance dose following an initial period of conventional dose therapy appears to reduce toxicity (thereby improving patient tolerability) without compromising quality or durability of response.

439 LENALIDOMIDE TREATMENT – SAFE TO ADMINISTER TO CYTOPENIC PATIENTS

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Lenalidomide has displayed immunomodulatory effects in a wide range of diseases and is currently being trialled in various subtypes of Non Hodgkins Lymphoma; We have undertaken a phase II trial of its use in relapsed/refractory Mantle Cell Lymphoma. Mantle Cell Lymphoma accounts for 5% of Non Hodgkins lymphoma and is characterised by multiple relapses with short periods of remission. The effect of multiple lines of prior therapy often renders these patients cytopenic, often excluding them from receiving lenalidomide. We have administered a total of 157 cycles of lenalidomide within our trial (to date) with 85 of these cycles given to cytopenic patients (neutrophils <1.5 x10(9)/L, platelets <100 x10(9)/L or both). The trial dosing schedule was 25mg lenalidomide for 6 cycles and 15mg maintenance until disease progression / relapse. Of the 85 cycles given to cytopenic patients 79% (18/85) were given at protocol dose with no reductions. In detail, 42 cycles of treatment were given to patients with platelets under 100 x10(9)/L, of which 12 cycles were in patients with platelets under 60 x10(9)/L and 4 were in patients with platelets under 40 x10(9)/L. Only one patient had mild purpura (platelets 52 x10(9)/L). No bleeding was reported. 59 cycles of treatment were given to patients with neutrophils <1.5 x10(9)/L. 6 infections were reported, (12% cycles): only 1 infection necessitated hospital admission. The infection rate was comparable to that of the non neutropenic patients (14%), with hospitalisation being more frequent in the non neutropenic group. Of the 59 cycles given to neutropenic patients, 7 patients had neutrophils of <1.0 x10(9)/L at the start of the cycle. All of these patients received GCSF support (2-3 x a week) and no antibiotic prophylaxis. Only 1 respiratory infection was reported - the patient had oral antibiotics at home. 18 cycles of treatment were administered to patients with platelets <100 x10(9)/L AND neutrophils <1.5 x10(9)/L (3 of the patients had neutrophils <1.0 x10(9)/L). No cytopenic complications were reported in any of these patients. Lenalidomide administration is often limited by myelotoxicity however our data shows that it is safe to administer lenalidomide to patients with up to grade 3 neutropenia or thrombocytopenia. Adopting this strategy has allowed increased drug delivery to a heavily pretreated population of patients with no discernible increase in morbidity or mortality. We are now extending our trial to recruit cytopenic patients who will receive an escalating dosing schedule of lenalidomide beginning at 10mg and escalating to the standard dose of 25mg in order to increase drug delivery for these difficult to treat patients.