

Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is “None”, please specify “None” as your response. “Not applicable” is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** University of Pittsburgh- of the Commonwealth System of Higher Education
2. **Reporting Period (start and end date of grant award period):** 01/01/2010 – 12/31/2013
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Margaret C. McDonald, PhD
4. **Grant Contact Person’s Telephone Number:** 412-383-7474
5. **Grant SAP Number:** 4100050913
6. **Project Number and Title of Research Project:** 04 - Clinical Trials in Multiple Myeloma
7. **Start and End Date of Research Project:** 01/01/2010 – 12/31/2011
8. **Name of Principal Investigator for the Research Project:** Suzanne Lentzsch, MD, PhD
9. **Research Project Expenses.**

9(A) Please provide the total amount of health research grant funds spent on this project for the entire duration of the grant, including indirect costs and any interest earned that was spent:

\$ 460,054

9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project	Cost
Welsh, Ann	Clinical Research Coordinator (CRC)	50% (1/1/10-1/31/12)	\$97,710.01
Kennedy, Ryan	Clinical Research Associate (CRA)	65% (1/1/10-12/31/11); 1.54% (1/1/12-1/31/12)	\$61,731.52
Richard, Donald	CRA	40% (1/1/10-1/31/12)	\$60,209.45
O'Sullivan, Amy	CRC	65% (1/1/10-10/24/10)	\$41,362.24
Marin, Emily	CRC	65% (2/13/11-1/31/12)	\$41,302.83

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project
Lentzsch, Suzanne	Principal Investigator	5%
Normolle, Daniel	Biostatistician	3%
Mapara, Markus	Co-Investigator	1%
Gollin, Susanne	Co-Investigator	1%
Boyiadzis, Michael	Co-Investigator	1%
Roodman, David	Co-Investigator	1%
Agha, Mounzer	Co-Investigator	1%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
None		

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes X No _____

If yes, please indicate the source and amount of other funds:

UPCI 07-089: Cephalon \$256,400

UPCI 07-134: Celgene \$128,880

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes _____ No X _____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert “not funded” in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
None	<input type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify: __)		\$	\$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes _____ No X _____

If yes, please describe your plans:

12. Future of Research Project. What are the future plans for this research project?

UPCI 07-089: A group of investigators in Ireland is currently repeating this study, which is expected to provide independent analyses that may potentially support our findings.

UPCI 07-134: Patients with multiple myeloma are living longer than anticipated when this study was originally designed. Longevity is largely attributable to approval of novel therapies, including lenalidomide. Subjects will continue to be followed for progression-free survival (PFS) and overall survival (OS) for the next several years so that data can mature

and PFS and OS can be analyzed.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes _____ No X _____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				
Other				
Unknown				
Total				

14. Recruitment of Out-of-State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes _____ No X _____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes X _____ No _____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

We developed and implemented a data capture system for multiple myeloma that continues to be used for investigator-initiated clinical trials in myeloma at the University of Pittsburgh Cancer Institute.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes X No _____

If yes, please describe the collaborations:

These studies have led to a collaboration with oncologists and biostatisticians at Columbia University in New York, NY, as well as Karmanos Cancer Institute in Detroit, MI.

16(B) Did the research project result in commercial development of any research products?

Yes _____ No X _____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes _____ No X _____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant agreement). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations

at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (β) should not print as boxes (\square) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

UPCI 07-089: Phase I Study of Bendamustine in Combination with Lenalidomide (CC-5013) and Dexamethasone in Patients with Refractory or Relapsed Multiple Myeloma

This phase 1/2 trial investigated the combination of bendamustine, lenalidomide, and dexamethasone in repeating 4-week cycles as treatment for relapsed refractory multiple myeloma (MM). The primary objective was to determine the safety and maximum tolerated dose (MTD) of bendamustine and lenalidomide in combination with a fixed dose of dexamethasone for patients with refractory or relapsed multiple myeloma. Secondary objectives were to: 1) establish the dose of each drug recommended for a future Phase II protocol with the combination; 2) explore anti-tumor activity of the combination of bendamustine plus lenalidomide and dexamethasone; and 3) examine toxicity, time to progression, and overall survival.

Enrollment for this study was completed on January 7, 2011, when target accrual was met. In total, 36 subjects were screened with seven screen failures for a total of 29 subjects enrolled in the trial. Median age was 63 (range, 38-80 years). Median number of prior therapies was three (range, 1-6). Maximum tolerated dose (MTD) was bendamustine 75 mg/m² (days 1 and 2), lenalidomide 10 mg (days 1-21), and dexamethasone 40 mg (weekly) of a 28-day cycle. Partial response rate was 52%, with very good partial response achieved in 24%, and minimal response in an additional 24% of patients. Median follow-up was 13 months; median overall survival (OS) has not been reached. One-year OS is 93% (95% confidence interval, 59%-99%, Figure 1). Median progression free survival (PFS) is 6.1 months (95% CI, 3.7-9.4 months) with one-year

PFS of 20% (95% CI, 6%-41%, Figure 1). Grade 3/4 adverse events included neutropenia, thrombocytopenia, anemia, hyperglycemia, and fatigue. In summary, this first phase 1/2 trial testing bendamustine, lenalidomide, and dexamethasone (BLD) as treatment of relapsed refractory multiple myeloma (MM) was feasible and highly active. These results (and detailed methods) were published in the journal *Blood* (2012 May 17;119(20):4608-13).

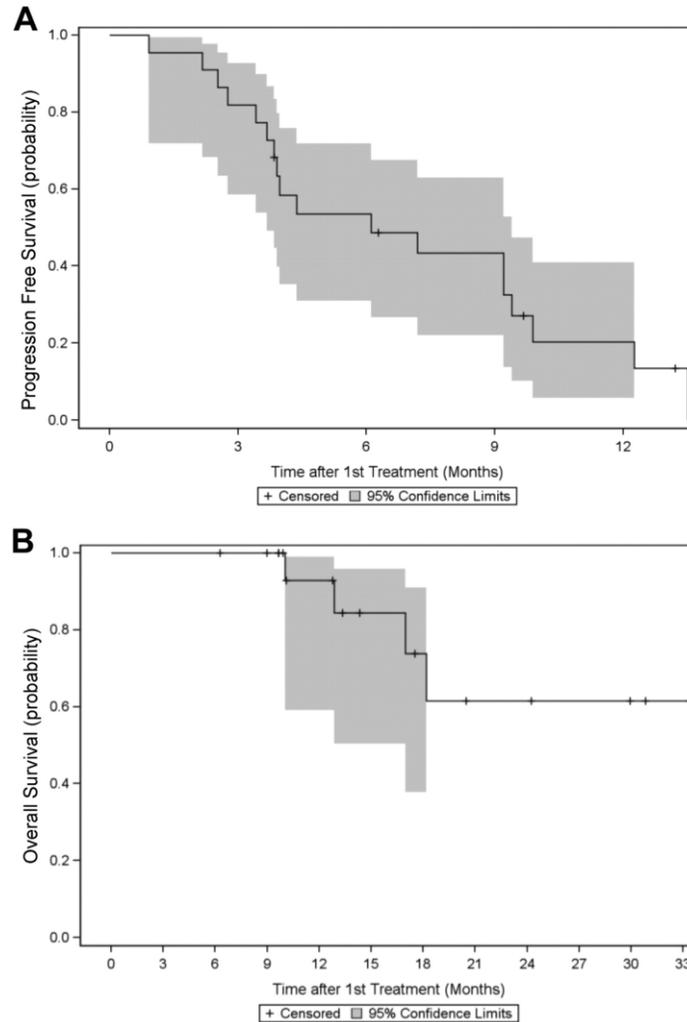


Figure 1. Progression free survival and overall survival. Kaplan-Meier estimates (in months) with 95% CI of (A) PFS and (B) OS in 25 patients treated with BLD for relapsed MM.

UPCI 07-134: A Randomized Clinical Trial of Lenalidomide (CC-5013) and Dexamethasone with and without Autologous Peripheral Blood Stem Cell Transplant in Patients with Newly Diagnosed Multiple Myeloma

The primary objectives of this trial were to estimate the complete response rate in newly diagnosed multiple myeloma patients receiving an autologous peripheral blood stem cell transplant after undergoing four cycles of lenalidomide and low-dose dexamethasone (Arm A) compared to patients receiving six to eight cycles of lenalidomide and low-dose dexamethasone until plateau of best response (Arm B). The secondary objectives were to: 1) compare the overall response rate induced by lenalidomide and dexamethasone to the response induced by lenalidomide and dexamethasone followed by an autologous peripheral blood stem cell transplant; 2) determine if there is a benefit in progression-free survival in patients receiving an autologous peripheral blood stem cell transplant after undergoing four cycles of lenalidomide and dexamethasone compared to patients receiving six to eight cycles of lenalidomide and dexamethasone until plateau of best response; 3) compare overall survival and time to progression in patients receiving an autologous peripheral blood stem cell transplant after undergoing induction therapy with lenalidomide and dexamethasone compared to patients receiving only lenalidomide and dexamethasone; and 4) compare the toxicity of lenalidomide and dexamethasone followed by an autologous peripheral blood stem cell transplant to lenalidomide and dexamethasone alone.

This study met the accrual target, with one patient on active treatment at the end of 2013. All patients will complete the treatment phase of the protocol by the end of 2014 and will be evaluated for response. Patients with multiple myeloma are living longer than anticipated when this study was originally designed. Longevity is largely attributable to the approval of novel therapies, including lenalidomide. Subjects will be followed for PFS and OS for the next several years so that data can mature and PFS and OS can be analyzed. However, the following interim study results of this trial were presented at the 55th American Society of Hematology Annual Meeting and Exposition on December 7-10, 2013 in New Orleans, LA:

Fifty-eight (58) subjects were screened with fifty (50) eligible to commence on the randomized treatment arm. Twenty-four (24) subjects were randomized and treated with lenalidomide (CC-5013) and dexamethasone (Ld) with autologous stem cell transplant (ASCT) [Arm A] and twenty-six (26) were randomized to lenalidomide (CC-5013) and dexamethasone (Ld) [Arm B]. With compelling results of a national cooperative clinical trial, the study was modified to include peripheral stem cell harvesting in Arm B and maintenance lenalidomide (CC-5013) in Arm A and Arm B.

Of the 50 randomized patients, 47 were eligible for evaluation in this interim analysis (25 in Arm A and 22 in Arm B). Reasons for ineligibility were non-compliance with the study regimen (N=2) and nursing home admission (N=1). Baseline characteristics of the analysis population are shown in Table 1. The median age of all patients was 61.6 years (range 48-75). Overall, 60% of patients were male, and 34%, 49%, and 17% had International Staging System (ISS) stage I, II, and III disease, respectively.

Table 1. Baseline patient characteristics.

	Ld+ASCT (N=25)	Ld alone (N=22)
Median age, years (range)	61.8 (48.0–75.1)	61.0 (50.3–72.4)
Gender, n (%)		
Male	14 (56.0)	14 (63.6)
Female	11 (44.0)	8 (36.4)
Race, n (%)		
White	20 (80.0)	17 (77.3)
African-American	3 (12.0)	4 (18.2)
Other	2 (8.0)	1 (4.5)
ECOG performance status, n (%)		
0	12 (48.0)	11 (50.0)
1	13 (52.0)	10 (45.5)
2	0	1 (4.5)
ISS stage, n (%)		
I	9 (36.0)	7 (31.8)
II	11 (44.0)	12 (54.6)
III	5 (20.0)	3 (13.6)

ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System

The median follow-up time was 36.8 months (range 1.1-62.7) in the total population, 34.7 months (range 1.1-57.6) in Arm A, and 37.1 months (range 1.6-62.7) in Arm B. A trend toward an improved overall response rate (ORR) was observed in Arm A vs. Arm B (96.0% vs. 77.3%, $p=0.08$; Table 2). The median duration of response was 13.9 months (95% CI: 4.0-34.1) in Arm A and 21.2 months (95% CI: 11.0-22.9) in Arm B. This difference was not statistically significant.

Table 2. Best response to therapy.

Best response, n (%)	Ld+ASCT (N=25)*	Ld alone (N=22)*
SCR	1 (4.0)	1 (4.6)
CR	4 (16.0)	5 (22.7)
VGPR	8 (32.0)	6 (27.3)
PR	11 (44.0)	5 (22.7)
SD	1 (4.0)	5 (22.7)
PD	0	0
ORR [†]	24 (96.0) [‡]	17 (77.3) [‡]

CR, complete response; ORR, overall response rate; PD, progressive disease; PR, partial response; SCR, stringent complete response; SD, stable disease; VGPR, very good partial response
^{*} $p=0.25$ for comparison of the distribution of response categories between treatment arms (Fisher's exact test); [†]SCR+CR+VGPR+PR; [‡] $p=0.08$ for comparison between treatment arms (Fisher's exact test)

At the last follow-up in this analysis, 18 patients had progressive disease (PD) (Arm A, N=10; Arm B, N=8) and 8 had died (Arm A, N=4; Arm B, N=4). Seven of the deaths were due to MM; one was due to heart disease.

There was no significant difference in PFS or OS between treatment arms (Table 3; Figures 2 and 3).

Table 3. Median PFS and OS in patients treated with Ld+ASCT vs. Ld alone.

	Ld+ASCT (N=25)	Ld alone (N=22)	p value (log-rank test)
Median PFS, months (95% CI)	17.0 (15.5–not estimable)	25.2 (9.0–not estimable)	0.94
Median OS, months (95% CI)	57.6 (48.0–not estimable)	Not reached	0.97

Figure 2. Progression-free survival.

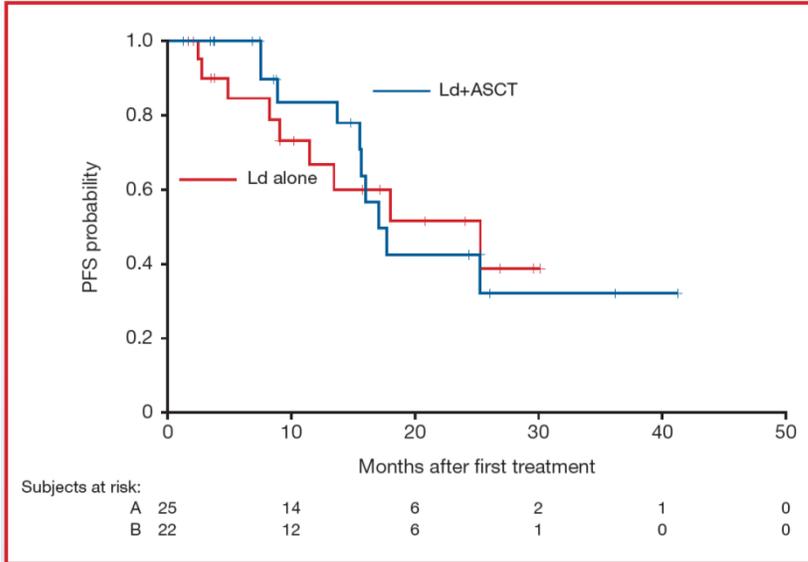
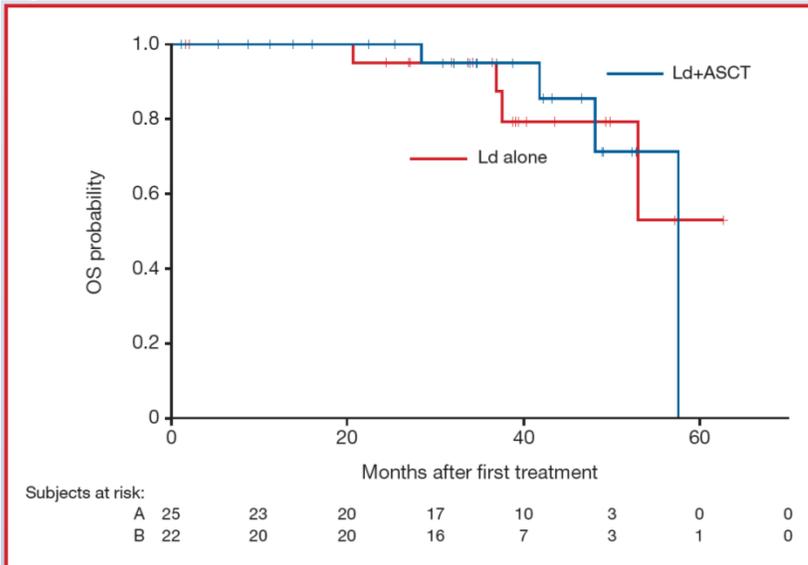


Figure 3. Overall survival.



Conclusions: This interim analysis of an ongoing, randomized clinical study suggests that addition of ASCT to Ld may improve ORR vs. Ld alone in patients with newly diagnosed MM. In contrast, a trend towards improved duration of response in the Ld alone arm was observed. The apparent improvement in ORR with the addition of ASCT to Ld did not result in a statistically significant improvement in PFS or OS vs. Ld alone. These findings suggest that Ld alone can achieve similar results to Ld+ASCT; however, in view of the low patient numbers and relatively short follow-up, care is required in the interpretation of the data.

In addition to these interim analyses regarding survival, toxicity data were collected and analyzed for all patients enrolled in this study. There were no findings that diverged from those already noted in the package inserts for the drugs used in this study. However, approximately three years ago, investigators began following the development of myelodysplastic syndrome (MDS) and other secondary malignancies as adverse events of lenalidomide treatment in patients with MM. These data are being collected for all subjects on this protocol, and the findings regarding MDS from this trial were reported in the journal *Leukemia & Lymphoma* (2013 Sept; 54(9):1965-74). Briefly, bone marrow morphology and cytogenetics studies from 40 patients were evaluated for early signs of MDS prior to therapy, during therapy, and at follow-up. One patient developed MDS. Baseline prevalence of mild morphologic myelodysplasia was highest in pretreated patients with MM (71%), but was also seen in the newly diagnosed patients from Arms A and B of this trial (17%). The prevalence of myelodysplasia did not increase over time. Thus, this study did not reveal rapidly emerging MDS in 39 of 40 patients with MM treated with lenalidomide, and it is therefore likely that the benefit of lenalidomide maintenance therapy outweighs the risk of secondary cancer development for the majority of MM patients. Larger studies with longer follow-up are needed to confirm these results. Using newer molecular genetic assays, future studies may also be able to identify which patients with MM are particularly prone to develop MDS when being treated with specific therapies, possibly including lenalidomide, and may provide information to better tailor therapy for individual patients.

Dr. Suzanne Lentzsch left the University of Pittsburgh in February 2012 but continues this important line of research from her new position as Director of the Multiple Myeloma and Amyloidosis Service at New York Presbyterian Hospital/Columbia University Medical Center.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be “No.”

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

Yes (two studies: UPCI 07-134 and UPCI 07-089)

No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

 X Yes (While UPCI 07-134 is still underway, UPCI 07-089 has been completed.)

 No

If “Yes” to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both “No.”)

18(C) How many hospital and health care professionals were involved in the research project?

 20 Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

 93 Number of subjects originally targeted to be included in the study

 79 Number of subjects enrolled in the study

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:

 44 Males

 32 Females

 3 Unknown

Ethnicity:

 Latinos or Hispanics

 Not Latinos or Hispanics

 79 Unknown

Race:

 American Indian or Alaska Native

 Asian

 7 Blacks or African American

 Native Hawaiian or Other Pacific Islander

 37 White

 Other, specify: _____

 35 Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

These trials were based at the Hillman Cancer Center in Allegheny County, but participating patients were also treated at sites throughout the UPMC CancerCenter network, including Somerset, Mercer, Lawrence, Butler, Beaver, Washington, Westmoreland, Fayette, and Indiana Counties.

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?

Yes
 No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?

Yes
 No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, and an abbreviated title of the publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04), the filenames would be:

Project 01 – Smith – Three cases of isolated
Project 01 – Smith – Investigation of NEB1 deletions
Project 03 – Zhang – Molecular profiling of aromatase

Project 04 – Bates – Neonatal intensive care
 If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. Combination of bendamustine, lenalidomide, and dexamethasone (BLD) in patients with relapsed or refractory multiple myeloma is feasible and highly effective: results of phase ½ open-label, dose escalation study	Suzanne Lentzsch, Amy O’Sullivan, Ryan C. Kennedy, Mohammad Abbas, Lijun Dai, Silvana Lalo Pregja, Steve Burt, Michael Boyiadzis, G. David Roodman, Markus Y. Mapara, Mounzer Agha, John Waas, Yongli Shuai, Daniel Normolle, and Jeffrey A. Zonder	Blood	November 2011	<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input checked="" type="checkbox"/> Published
2. Longitudinal bone marrow evaluations for myelodysplasia in patients with myeloma before and after treatment with lenalidomide	Sara A. Monaghan, Lijun Dai, Markus Y. Mapara, Daniel P. Normolle, Susanne M. Gollin, and Suzanne Lentzsch	Leukemia & Lymphoma	July 2012	<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input checked="" type="checkbox"/> Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes X No _____

If yes, please describe your plans:

UPCI 07-134: Once the data matures, we plan to publish results from our final analyses in a peer-reviewed journal.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project.

Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis,

or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

Results from this research project inform clinicians on treatment options for patients with multiple myeloma and therefore may impact patient care.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

We have demonstrated that the combination of bendamustine, lenalidomide, and dexamethasone is a highly active regimen for patients with relapsed or refractory multiple myeloma, where 76% of patients had some degree of objective improvement.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No X

If “Yes” to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is “No.”)

- a. Title of Invention:
- b. Name of Inventor(s):
- c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):
- d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No_____

If yes, indicate date patent was filed:

- e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No_____

If yes, indicate number of patent, title and date issued:

Patent number:

Title of patent:

Date issued:

- f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes _____ No _____

If yes, how many licenses were granted? _____

- g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes ___ No ___

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes _____ No X _____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages.

BIOGRAPHICAL SKETCH

NAME Suzanne Lentzsch, MD, PhD	POSITION TITLE Associate Professor of Medicine
eRA COMMONS USER NAME (credential, e.g., agency login) lentzsch	

EDUCATION/TRAINING

<u>INSTITUTION AND LOCATION</u>	<u>DEGREE</u> <i>(if applicable)</i>	<u>MM/YY</u>	<u>FIELD OF STUDY</u>
Humboldt University Berlin, Germany	MD	07/90	Medicine
Humboldt University Berlin, Germany	PhD	03/94	Medicine
Humboldt University Berlin, Germany	Residency	11/98	Internal Medicine
Humboldt University Berlin, Germany	Fellowship	06/04	Hematology/Oncology

A. Personal Statement

I have a broad background in multiple myeloma and amyloidosis with an expertise in translational research. As a postdoctoral fellow in the laboratory of Dr. Kenneth Anderson at the Dana-Farber Cancer Institute, Boston, I was the first who studied the effects of Immunomodulatory drugs (IMiDs) such as lenalidomide *in vivo*. At the University Medical Center Charité, Department of Hematology, Medical Oncology and Tumorimmunology, Berlin, Germany I continued my basic research on IMiDs and also became the National PI in Germany for the international trial MM 010 “Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma.” As the Clinical Director of the Multiple Myeloma Program at the University of Pittsburgh and Director of the Multiple Myeloma and Amyloidosis Service at Columbia University, New York (since 2012), I established a robust translational research program including basic and clinical research. One of my investigator-sponsored phase 1/2 trials laid the groundwork for now successfully using IMiDs in new combinations to improve the response rates in multiple myeloma. My high interest in translational research and bringing our findings from bench to bedside is further reflected by the fact that my research laboratory is NIH funded and engages 3 postdocs. Further, I am the PI of several industry- and consortium-sponsored trials including 3 investigator-sponsored trials. One of the investigator-sponsored trials is a phase 2 multicenter trial testing the efficacy of Bendamustine in AL Amyloidosis. As the PI of this trial, I am supervising and coordinating 5 academic sub-sites. I successfully oversee critical parts of the study such as auditing, data management, safety and adverse event reporting, staffing, research protections and budget.

B. Positions and Employment

09/1990 – 12/1999 Residency/Fellowship, Humboldt University, University Medical Center Charité, Dept of Hematology, Medical Oncology and Tumor Immunology, Berlin, Germany

01/2000 – 02/2001 Research Fellowship, Dana-Farber Cancer Institute, Department of Adult Oncology, Harvard Medical School, Boston, MA

02/2001 – 07/2004 Fellowship, Humboldt University, University Medical Center Charité, Department of Hematology, Medical Oncology and Tumor Immunology, Berlin, Germany

08/2004 – 06/2011 Asst. Professor of Medicine, University of Pittsburgh Cancer Institute, Division of Hematology and Oncology, Pittsburgh, PA

07/2007 – 02/2012 Clinical Director, Multiple Myeloma Program, University of Pittsburgh Cancer Institute, Division of Hematology and Oncology, Pittsburgh, PA

07/2011 – 02/2012 Associate Professor of Medicine, University of Pittsburgh Cancer Institute, Division of Hematology and Oncology, Pittsburgh, PA

03/2012 – present Associate Professor of Clinical Medicine, Columbia University Medical Center, Department of Medicine, Division of Hematology/Oncology, New York, NY

03/2012 – present Director, Multiple Myeloma Service, Columbia University Medical Center, Department of Medicine, Division of Hematology/Oncology, New York, NY

C. Selected Peer-Reviewed Publications

1. Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. Richardson PG, Siegel DS, Vij R, Hofmeister CC, Baz R, Jagannath S, Chen C, Lonial S, Jakubowiak A, Bahlis N, Song K, Belch A, Raje N, Shustik C, **Lentzsch S**, Lacy M, Mikhael J, Matous J, Vesole D, Chen M, Zaki MH, Jacques C, Yu Z, Anderson K. Blood. 2014 Jan 13.
2. International Myeloma Working Group recommendations for global myeloma care. Ludwig H, Miguel JS, Dimopoulos MA, Palumbo A, Garcia Sanz R, Powles R, **Lentzsch S**, Ming Chen W, Hou J, Jurczyszyn A, Romeril K, Hajek R, Terpos E, Shimizu K, Joshua D, Hungria V, Rodriguez Morales A, Ben-Yehuda, D, Sondergeld P, Zamagni E, Durie B. Leukemia. 2013 Oct 9.
3. Lenalidomide-induced upregulation of CXCR4 in CD34+ hematopoietic cells, a potential mechanism of decreased hematopoietic progenitor mobilization. Li S, Fu J, Ma H, Mapara MY, **Lentzsch S**. Leukemia. 2013 Jun;27(6):1407-11.

D. Ongoing Research Support

R01 CA175313-01 The role of MMP13 in Multiple Myeloma Bone Disease The goal of this study is to investigate the whether MMP13 secreted by myeloma cells induce osteoclast activity and subsequently the development of lytic lesions.	Lentzsch (PI)	2013-2018
Leukemia and Lymphoma Society, LLS 6096-10 Effects of IMiDs on Granulocytic Maturation The goal of this study is to evaluate the effects of IMiDs on myeloid precursors to investigate the potential increased risk of secondary hematologic malignancies in patients treated with IMiDs.	Lentzsch (PI)	03/01/09-09/30/14
ASH 2013 Bridge Grant Award The Role of MMP13 in Multiple Myeloma Bone Disease This is a bridge funding was based on the initial R01 application and hence the goal of this study is similar to the one of the R01 application.	Lentzsch (PI)	04/01/13-03/31/14
International Myeloma Foundation The role of C/EBPbeta as a potential target for the treatment of multiple myeloma The goal of this project is to identify new treatment targets for multiple myeloma.	Lentzsch (PI)	2012-2014
Celgene Corporation Effect of IMiD® Immunomodulatory drugs on Megakaryopoiesis” Identifying critical targets of IMiD® Immunomodulatory drugs might further contribute to the development of predictors of thrombocytopenia.	Lentzsch (PI)	2009-2014
Celgene Corporation Investigator Initiated Trial AAA J2355: A randomized clinical phase 3 trial of lenalidomide and dexamethasone with and without autologous peripheral blood stem cell transplant in patients with newly diagnosed multiple myeloma.	Lentzsch (PI)	2009-2014
Cephalon/Teva Pharmaceuticals Investigator Initiated Trial AAA J7800: Multicenter phase 2 study of Bendamustine and dexamethasone in patients with refractory amyloidosis.	Lentzsch (PI)	2012-2015
Onyx Pharmaceuticals Investigator Initiated Trial AAA J2359: Phase I/II study of Carfilzomib in combination with Bendamustine and dexamethasone in patients with newly diagnosed multiple myeloma.	Lentzsch (PI)	2013-2015
Novartis (awarded not funded yet) Investigator Initiated Trial AAA J2359: Phase 2 study of the IGF-1R inhibitor SOM230 in combination with Carfilzomib for relapsed or refractory multiple myeloma.	Lentzsch (PI)	