

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):** 01/01/2009 – 12/31/2012
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Margaret C. McDonald, Ph.D.
4. **Grant Contact Person’s Telephone Number:** 412-383-7474
5. **Grant SAP Number:** 4100047655
6. **Project Number and Title of Research Project:** 03 – Clinical Trials in Melanoma
7. **Start and End Date of Research Project:** 01/01/2009 – 12/31/2010
8. **Name of Principal Investigator for the Research Project:** John Kirkwood, MD
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:

\$ 506,413.07

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	Position Title	% of Effort on Project	Cost
Horak	Clinical Research Associate	41% Yr 1; 85% Yr 2; 33% Yr 3	\$ 77,281
Hahn-Efrati	Senior Regulatory Specialist	29.6% Yr 1; 40% Yr 2; 29.2% Yr 3	\$ 52,544
Merriman	Clinical Research Associate	41.7% Yr 1; 100% Yr 2; 41.7% Yr 3	\$ 94,955
Rose	Clinical Research Coordinator	1.7% Yr 1	\$ 941
Mays	Senior Regulatory Specialist	35% Yr 1; 85% Yr 2; 35% Yr 3	\$105,674

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	Position Title	% of Effort on Project
Kirkwood	Principal Investigator	5%
Tarhini	Co-Investigator	5%
Tawbi	Co-Investigator	5%

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 No

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

Eastern Cooperative Oncology Group (ECOG) Main Institution NIH U10CA39229-26
\$164,857 (annual direct costs)

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 X No _____

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:
ECOG Main Institution	<input checked="" type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify:_____) <input type="checkbox"/> Nonfederal source (specify:_)	06/2009	\$1,352,496	\$1,098,287
ECOG Prevention Member	<input checked="" type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify:_____) <input type="checkbox"/> Nonfederal source (specify:_)	06/2011	\$311,244	\$311,244

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

Yes X No _____

If yes, please describe your plans:

NIH U10CA39229 ECOG Main Institution (continue)
NIH U10CA037403 ECOG Prevention Member (continue)

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

New trials are proposed (E3611) or already launched (E1609) that have benefited from the knowledge gained in E1697.

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

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

	Undergraduate	Masters	Pre-doc	Post-doc
Male	1		1	
Female				
Unknown				
Total	1		1	

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic	1		1	
Unknown				
Total	1		1	

	Undergraduate	Masters	Pre-doc	Post-doc
White			1	
Black				
Asian	1			
Other				
Unknown				
Total	1		1	

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

Yes No

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

Vishnu Chandra, Biological Sciences and Psychology, Minor in Biomedical Engineering and Chemistry 2009 – 2013 (expected) , Carnegie Mellon University. Previous affiliation: Mayo Clinic.

Joseph Stuckert, MD is now a dermatology resident at the University Hospitals Case Medical Center. He attended the University of Pittsburgh and obtained his BS in neuroscience in 2003 and MD in 2009. He joined UPMC for his preliminary medicine in 2009.

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

Yes No

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

The support of research coordination for E1697 has improved the infrastructure for clinical research at the University of Pittsburgh Cancer Institute and increased our ability to carry out these new trials and the laboratory translational correlates of the research.

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 No

If yes, please describe the collaborations:

We have collaborated with Dr. Charalampos Floudas and Dr. Helen Gogas of the University of Athens for this research.

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

Yes No

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

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

Clinical trial participants has been active with affiliates of UPMC at Latrobe, Beaver, Erie and other sites of the UPCI ECOG affiliate network including Cumberland, MD, Wheeling, WV, Morgantown, WV, Charleston, WV, and Cincinnati, OH

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.

E1697 (UPCI 99-006): This study closed to accrual in fall 2010 after the third planned interim analysis with 1,150 subjects enrolled nationally. Primary endpoints of the trial were relapse-free survival (RFS) and overall survival (OS).

Of the 1150 patients enrolled, 581 were assigned to the interferon-alfa (IFN) treatment group and 596 to observation (Obs). A total of 91 subjects have been screened, and 64 have been enrolled at the University of Pittsburgh. The third interim analysis of this trial was carried out in August 2010 at 69.0% information time. The median RFS for Obs was 7.3 years (95% CI 5.3-9.8; n=413) while for IFN, RFS was 6.8 years (95% CI 5.1-9.0; n=425). The 5-year survival rate for Obs was 0.85 (95% CI 0.81-0.89; n=535) while for IFN induction-only, the 5-year survival rate was 0.82 (95% CI 0.78-0.86; n=556).

Futility analysis indicated low conditional power that one month of IFN may improve the outcome of patients enrolled on this study compared to observation. Therefore, we concluded that adjuvant HDI (high-dose interferon alpha) induction with only 4 weeks therapy neither improved RFS nor OS over observation for patients with intermediate and high-risk melanoma. This trial supports the importance of HDI treatment duration and argues that the approved one year interferon regimen of induction followed by maintenance remains the standard of care for patients with T4NO or node positive disease.

The first report from this study was presented at the 2011 American Society of Clinical Oncology (ASCO) Annual Meeting (Argawala et al., J Clin Oncol 2011). Coordination efforts at UPCI continue to include patient follow-up of currently enrolled subjects as well as banking of nationally collected blood samples for the ongoing corollary biomarker studies.

E2602 (UPCI 03-111): This is a phase II study of peginterferon alfa-2b in subjects with metastatic melanoma over-expressing the basic fibroblast growth factor (b-FGF). The primary objective is to suppress the plasma b-FGF level to normal (≤ 7.5 pg/mL) with low dose peginterferon alfa-2b. Secondary objectives are: (1) to estimate the anti-tumor effect of peginterferon alfa-2b in terms of progression-free survival, overall survival, and tumor response; (2) to correlate tumor activity with b-FGF and VEGF levels in the plasma and urine; and (3) to study the safety profile of peginterferon alfa-2b in metastatic melanoma. UPCI has contributed the largest number of patients to this trial. This study has been permanently closed to accrual since November 2012.

The study analysis will be submitted to the 2013 ASCO Annual Meeting.

UPCI 05-125: To date, UPCI has enrolled 37 patients, completing accrual for this trial. The hypothesis tested was that the combination of tremelimumab and interferon alfa-2b acting via different and possibly synergistic mechanisms would overcome tumor immune tolerance and lead to significant and durable clinical responses. We have concluded that HDI can be administered in combination with tremelimumab with acceptable toxicity and promises durable antitumor efficacy that warrants further testing in a randomized trial. It therefore met the phase II criteria for efficacy. Results of this study have been published in the *Journal of Clinical Oncology*, January 2012 (Tarhini et al, JCO Jan 2012).

UPCI 07-008: This Phase I/II trial was completed in 2010, and a total of 39 patients were accrued on this study. This study demonstrated that decitabine (DAC) can safely be added to temozolomide (TMZ) in patients with metastatic melanoma at biologically relevant doses, and the combination seems to reverse the resistance of melanoma to chemotherapy and thereby significantly improves the efficacy of chemotherapy in patients with metastatic melanoma. Analysis has concluded that the combination of DAC and TMZ is safe and leads to an 18% objective response rate and 12.4-month median OS, suggesting possible superiority over the historical 1-year OS rate, and warrants further evaluation in a randomized setting as published in the *Annals of Oncology*, November 2012 (Tawbi HA et al Annals Onc Nov 2012).

The following papers were published from the work conducted with the project funds, but acknowledgment of the Pennsylvania Department of Health funding was inadvertently omitted:

1. Tarhini AA, Cherian J, Moschos SJ, Tawbi HA, Shuai Y, Gooding WE, Sander C, Kirkwood JM. Safety and efficacy of combination immunotherapy with interferon alfa-2b and tremelimumab in patients with stage IV melanoma. J Clin Oncol. 2012 Jan 20;30(3):322-8. (UPCI 05-125)

2. Tawbi HA, Beumer JH, Tarhini AA, Moschos S, Buch SC, Egorin MJ, Lin Y, Christner S, Kirkwood JM. Safety and efficacy of decitabine in combination with temozolomide in metastatic melanoma: a phase I/II study and pharmacokinetic analysis. Ann Oncol. 2013 Apr;24(4):1112-9.

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
 No

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

Yes
 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?

235 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?

350 Number of subjects originally targeted to be included in the study
284 Number of subjects enrolled in the study

Note: 154 subjects determined to be eligible

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:

178 Males
106 Females
 Unknown

Ethnicity:

 Latinos or Hispanics
284 Not Latinos or Hispanics
 Unknown

Race:

 American Indian or Alaska Native
1 Asian
 Blacks or African American
 Native Hawaiian or Other Pacific Islander
254 White
 Other, specify: _____
29 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.)

Allegheny County

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
X 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, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the “Cognition and MRI in Older Adults” research project (Project 1), and two publications for PI Zhang for the “Lung Cancer” research project (Project 3), the filenames should be:

- Project 1 – Smith – Publication 1 – Cognition and MRI
- Project 1 – Smith – Publication 2 – Cognition and MRI
- Project 3 – Zhang – Publication 1 – Lung Cancer
- Project 3 – Zhang – Publication 2 – Lung Cancer

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. None				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input 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:

Final summary publications of the results of E1697 Phase III intergroup trial (Argawala,...Kirkwood) is in preparation for 2013, as is the final summary of the E2602 Phase II trial (Go, ...Kirkwood) for this year.

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.

E1697 has established the lack of adjuvant efficacy for 1 month HD-IFN α

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.

None

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 John M. Kirkwood, M.D.	POSITION TITLE
eRA COMMONS USER NAME	Professor of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Oberlin College, Oberlin, OH	B.A.	06/69	Biochemistry
Yale University School of Medicine, New Haven, CT	M.D.	06/73	Medicine
Yale University School of Medicine, New Haven, CT	Int./Res.	06/76	Internal Medicine
Harvard University, Boston, MA	Fellowship	06/78	Tumor Immunology

Positions and Honors

Positions and Employment

- 1967-1969 Senior Scholar in Tumor Immunology, Memorial Sloan Kettering, New York, NY
- 1976-1978 Assistant in Medicine, Peter Bent Brigham Hospital, Boston, MA
- 1978-1983 Assistant Professor of Medicine, Yale Univ. School of Medicine, New Haven, CT
- 1978-1986 Attending Physician, Yale University School of Medicine, New Haven, CT
- 1978-1986 Consultant - Attending, West Haven VA Hospital, West Haven, CT
- 1983-1986 Associate Professor of Medicine and Dermatology, Yale Univ. School of Med, New Haven, CT
- 1985-1986 Roosevelt Fellow/Visiting Scientist, Instituto per Tumori, Milan, Italy
- 1986-1993 Associate Director for Medical Oncology, Univ. of Pittsburgh Cancer Institute, Pittsburgh, PA
- 1986-1996 Professor and Chief, Div. of Med. Oncol, Department of Medicine, Univ. of Pittsburgh. Pgh, PA
- 1993- Director, Melanoma and Skin Cancer Program Center, Univ. of Pittsburgh Cancer Institute, Pittsburgh, PA
- 1996-2006 Professor and Vice Chairman for Clinical Research, Dept. of Med, Univ. of Pittsburgh, Pittsburgh, PA
- 2009- Professor of Clinical and Translational Science, University of Pittsburgh Clinical and Translational Science Institute

Honors

- 1989 Scientific Advisory Board, Cancer Research Institute, New York, NY
- 1996 UPCI Scientific Leadership Award, University of Pittsburgh Cancer Institute, Pittsburgh, PA
- 2000 ISICR Milstein Award, Amsterdam, The Netherlands
- 2005 Wings of Hope Award, New York, NY
- 2005 European Society of Cytokine Research Award
- 2008 Donald Wade Waddell Award, University of Arizona
- 2010 Wallace H. Clark Jr., MD Lecturer in Cutaneous Oncology

Selected Peer-Reviewed Publications

1. Moschos SJ, Edington HD, Land SR, Rao UN, Jukic D, Shipe-Spotloe J, **Kirkwood JM**. Neoadjuvant treatment of regional stage IIIB melanoma with high-dose interferon alfa-2b induces objective tumor regression in association with modulation of tumor infiltrating host cellular immune responses. *J Clin Oncol.* 2006 Jul 1;24(19):3164-71. PubMed PMID: 16809739.
2. Gogas H, Ioannovich J, Dafni U, Stavropoulou-Giokas C, Frangia K, Tsoutsos D, Panagiotou P, Polyzos A, Papadopoulos O, Stratigos A, Markopoulos C, Bafaloukos D, Pectasides D, Fountzilias G, **Kirkwood JM**. Prognostic significance of autoimmunity during treatment of melanoma with interferon. *N Engl J Med.* 2006 Feb 16;354(7):709-18. PubMed PMID: 16481638.
3. Tarhini AA, **Kirkwood JM**, Gooding WE, Moschos S, Agarwala SS. A Phase II trial of sequential temozolomide chemotherapy followed by high-dose interleukin 2 immunotherapy for metastatic melanoma. *Cancer* 2008 Oct 1;113(7):1632-40
4. Korn EL, Liu PY, Lee SJ, Chapman JA, Niedzwiecki D, Suman VJ, Moon J, Sondak VK, Atkins MB, Eisenhauer EA, Parulekar W, Markovic SN, Saxman S, **Kirkwood JM**. Meta-analysis of phase II cooperative group trials in metastatic stage IV melanoma to determine progression-free and overall survival benchmarks for future phase II trials. *J Clin Oncol.* 2008 Feb 1; 26(4):527-45. PMID: 18235113.
5. **Kirkwood JM**, Tarhini AA, Panelli MC, Moschos SJ, Zarour HM, Butterfield LH, Gogas HJ. Next generation of immunotherapy for melanoma. *J Clin Oncol.* 2008 Jul 10; 26(20):3445-55 PMID: 18612161
6. Wang W, Edington HD, Rao UN, Jukic DM, Radfar A, Wang H. **Kirkwood JM**. Effects of high-dose IFNalpha2b on regional lymph node metastases of human melanoma: modulation of STAT5, FOXP3, and IL-17. *Clin Cancer Res* 2008. Dec 15; 14(24):8314-20. PMID: 19088050.
7. Tarhini AA, Stuckert J, Lee S, Sander C, **Kirkwood JM**. Prognostic significance of serum S100B protein in high-risk surgically resected melanoma patients participating in Intergroup Trial ECOG 1694. *J Clin Oncol.* 2009 1;27(1):38-44.: PMID: 19047287. PMC3426933.
8. Tarhini AA, Cherian J, Moschos SJ, Tawbi HA, Shuai Y, Gooding WE, Sander C, **Kirkwood JM**. Safety and efficacy of combination immunotherapy with interferon alfa-2b and tremelimumab in patients with stage IV melanoma. *J Clin Oncol.* 2012;30(3):322-8. PMID: 22184371. PMC3422533.
9. **Kirkwood JM**, Butterfield LH, Tarhini AA, Zarour H, Kalinski P, Ferrone S. Immunotherapy of Cancer in 2012. *CA Cancer J Clin.* 2012 May 10. PMID: 22576456 . PMC3445708.
10. Tawbi HA, Beumer JH, Tarhini AA, Moschos SM, Buch SC, Egorin MJ, Lin Y, Christner S, **Kirkwood JM**. Safety and Efficacy of Decitabine in Combination with Temozolomide in Metastatic Melanoma: A Phase I/II Study and Pharmacokinetic Analysis. *Ann Oncol.* 2012 Nov 21. [Epub ahead of print] PMID: 23172636.
11. **Kirkwood JM**, Tarhini A, Sparano JA, Patel P, Schiller JH, Vergo MT, Benson Iii AB, Tawbi H. Comparative clinical benefits of systemic adjuvant therapy for paradigm solid tumors. *Cancer Treat Rev.* 2013 Feb;39(1):27-43. doi:10.1016/j.ctrv.2012.03.007. Epub 2012 Apr 19. PMID: 22520262.