**RCT**

**Potential PURL Review Form**

**PURL Jam Version**

**Version #11 October 29, 2009**

**Finally, a way to relieve cancer-related fatigue.**

***J Fam Pract*. 2014;63:270-272.**

**PURLs Surveillance System**

**Family Physicians Inquiries Network**

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| **SECTION 1: Identifying Information for Nominated Potential PURL** **[to be completed by PURLs Project Manager]** |
| **1.** Citation  | Wisconsin Ginseng (Panax quinquefolius) to Improve Cancer-Related Fatigue: A Randomized, Double-Blind Trial, N07C2.Barton DL, Liu H, Dakhil SR, Linquist B, Sloan JA, Nichols CR, McGinn TW, Stella PJ, Seeger GR, Sood A, Loprinzi CL.J Natl Cancer Inst. 2013 Aug 21;105(16):1230-8. doi: 0.1093/jnci/djt181. Epub 2013 Jul 13.PMID: 23853057 |
| **2.** Hypertext link to PDF of full article  | http://www.ncbi.nlm.nih.gov/pubmed/?term=Wisconsin+Ginseng+%28Panax+quinquefolius%29+to+Improve+Cancer-Related+Fatigue |
| **3.** First date published study available to readers  | 08/15/13 |
| **4.** PubMed ID  | 23853057 |
| **5.** Nominated By  | Other Other: Gary Asher |
| **6.** Institutional Affiliation of Nominator  | University of Missouri Other:  |
| **7.** Date Nominated  | 7/24/13 |
| **8.** Identified Through  | Other Other: TOC |
| **9.** PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland Other:  |
| **10.** Nomination Decision Date  | 8/15/13 |
| **11.** Potential PURL Review Form (PPRF) Type  | RCT |
| **12.** Other comments, materials or discussion  |  |
| **13.** Assigned Potential PURL Reviewer  | UNC, Gary Asher |
| **14.** Reviewer Affiliation  | Other Other: UNC |
| **15.** Date Review Due  | 11/8/13 |
| **16.** Abstract  | BACKGROUND:Safe, effective interventions to improve cancer-related fatigue (CRF) are needed because it remains a prevalent, distressing, and activity-limiting symptom. Based on pilot data, a phase III trial was developed to evaluate the efficacy of American ginseng on CRF.METHODS:A multisite, double-blind trial randomized fatigued cancer survivors to 2000 mg of American ginseng vs a placebo for 8 weeks. The primary endpoint was the general subscale of the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) at 4 weeks. Changes from baseline at 4 and 8 weeks were evaluated between arms by a two-sided, two-sample t test. Toxicities were evaluated by self-report and the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) provider grading.RESULTS:Three hundred sixty-four participants were enrolled from 40 institutions. Changes from baseline in the general subscale of the MFSI-SF were 14.4 (standard deviation [SD] = 27.1) in the ginseng arm vs 8.2 (SD = 24.8) in the placebo arm at 4 weeks (*P* = .07). A statistically significant difference was seen at 8 weeks with a change score of 20 (SD = 27) for the ginseng group and 10.3 (SD = 26.1) for the placebo group (*P* = .003). Greater benefit was reported in patients receiving active cancer treatment vs those who had completed treatment. Toxicities per self-report and CTCAE grading did not differ statistically significantly between arms.CONCLUSIONS:Data support the benefit of American ginseng, 2000 mg daily, on CRF over an 8-week period. There were no discernible toxicities associated with the treatment. Studies to increase knowledge to guide the role of ginseng to improve CRF are needed. |
| **17.** Pending PURL Review Date |  |
| **sECTION 2: Critical Appraisal of Validity****[to be completed by the Potential PURL Reviewer]****[to be revised by the Pending PURL Reviewer if needed]** |
| **1.** Number of patients starting each arm of the study? | 183 vs 181 |
| **2.** Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)? | Patients with cancer-related fatigue from 40 community cancer sites across the United States.Participants included both patients currently in treatment for cancer and patients who were posttreatment but within 2 years of diagnosis of their cancer. Eligible participants scored at least a 4 on a 0-10 visual analog scale (VAS), and had fatigue present for at least the past month. Patients with other causes of fatigue were excluded, as well as those who had pain or insomnia rated 4 or higher on a 0-10 VAS. Other patients excluded from the study included those with brain cancer, CNS lymphoma, current use of systemic steroids or opioids, as well as prior or current use of ginseng or other agents for fatigue. |
| **3.** Intervention(s) being investigated? | American ginseng root (Panax quinquefolius), 1000mg BID |
| **4.** Comparison treatment(s), placebo, or nothing? | Matched placebo capsule |
| **5.** Length of follow up? Note specified end points e.g. death, cure, etc. | 4 weeks (primary endpoint) and 8 weeks (secondary endpoints). |
| **6.** What outcome measures are used? List all that assess effectiveness. | Efficacy outcomes included:Multidimensional Fatigue Symptom Inventory – Short Form (MFSI-SF)Profile of Mood States (POMS)Brief Fatigue Inventory (BFI)CTCAE |
| **7.** What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, p-values, etc. | Greater reduction in fatigue score compared to placebo after 8 weeks: 20.0 vs 10.3, *p*=0.003 (on a 100 pt scale). |
| **8.** What are the adverse effects of intervention compared with no intervention? | No differences noted between groups. Nausea, vomiting, insomnia, anxiety, and agitation were the only adverse events (AEs) noted greater than 1%. |
| **9.** Study addresses an appropriate and clearly focused question - ***select one*** | [x]  Well covered [ ]  Adequately addressed [ ]  Poorly addressed[ ]  Not applicable Comments:  |
| **10.** Random allocation to comparison groups | [x]  Well covered [ ]  Adequately addressed [ ]  Poorly addressed [ ]  Not applicableComments:  |
| **11.** Concealed allocation to comparison groups | [ ]  Well covered [x]  Adequately addressed [ ]  Poorly addressed [ ]  Not applicableComments:  |
| **12.** Subjects and investigators kept “blind” to comparison group allocation | [ ]  Well covered [ ]  Adequately addressed [x]  Poorly addressed [ ]  Not applicableComments: Authors report a 'double-blind' design but do not mention who was blinded, nor how blinding was assessed. |
| **12.** Comparison groups are similar at the start of the trial | [x]  Well covered [ ]  Adequately addressed [ ]  Poorly addressed [ ]  Not applicableComments:  |
| **14.** Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias. | [x]  Well covered [ ]  Adequately addressed [ ]  Poorly addressed [ ]  Not applicableComments: Post randomization dropout a potential concern, but numbers were about equal for both groups, and participant characteristics between dropouts and other participants reported to be similar. No baseline differences between groups. |
| **15.** Were all relevant outcomes measured in a standardized, valid, and reliable way? | [ ]  Well covered [x]  Adequately addressed [ ]  Poorly addressed [ ]  Not applicableComments: Good description of outcome scales, but poorly described who collected data and whether they were masked (presumably yes d/t double-blind design). |
| **16.** Are patient oriented outcomes included? If yes, what are they? | Yes - fatigue |
| **17.** What percent dropped out, and were lost to follow up? Could this bias the results? How? | 6% post-randomization dropout, 12% dropout by 4 weeks (primary outcome), 24% dropout by 8 weeks. Dropout appears evenly divided between study arms. Many dropouts caused by AEs, which is common among cancer trials, and AEs did not appear to be caused by the study agent. |
| **18.** Was there an intention-to-treat analysis? If not, could this bias the results? How? | The authors do not specify intention to treat analysis, but they also don't report any crossover. It appears that all participants were analyzed based on the study arm they were randomized to (based on the CONSORT diagram). |
| **19.** If a multi-site study, are results comparable for all sites? | Authors do not report results by site (n=40). |
| **20.** Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity? | NCI and Breast Cancer Research Foundation unlikely sources of bias for this study. |
| **21.** To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized. | Any patients with cancer-related fatigue. |
| **22.** In what care settings might the findings apply, or not apply? | Primary Care, Cancer Survivorship care, Oncology. |
| **23.** To which clinicians or policy makers might the findings be relevant? | Primary care providers, oncologist and other cancer care providers. |
| **SECTION 3: Review of Secondary Literature****[to be completed by the Potential PURL Reviewer]****[to be revised by the Pending PURL Reviewer as needed]** |
| **Citation Instructions** | For UpTo Date citations, use style modified from <http://www.uptodate.com/home/help/faq/using_UTD/index.html#cite> & AMA style. Always use Basow DS as editor & current year as publication year.EXAMPLE: Auth I. Title of article. {insert author name if given, & search terms or title.} In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2009. Available at: <http://www.uptodate.com>. {Insert dated modified if given.} Accessed February 12, 2009. {whatever date PPRF reviewer did their search.}For DynaMed, use the following style:Depression: treatment {insert search terms or title}. In: DynaMed [database online]. Available at: <http://www.DynamicMedical.com>. Last updated February 4, 2009. {Insert dated modified if given.}  Accessed June 5, 2009.{search date} |
| **1.** DynaMed excerpts |  |
| **2.** DynaMed citation/access date | Title. Author. In: DynaMed [database online]. Available at: [www.DynamicMedical.com](http://www.DynamicMedical.com) Last updated: Accessed  |
| **3.**  Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences) |  |
| **4.** UpToDate excerpts |  |
| **5.** UpToDate citation/access date | Always use Basow DS as editor & current year as publication year. Title. Cancer-related fatigue: Treatment Author. AuthorCarmen P Escalante, MDSection EditorPaul J Hesketh, MDDeputy EditorDiane MF Savarese, MD In: UpToDate [database online]. Available at: <http://www.uptodate.com>. Last updated: 10/7/2013. Accessed 12/3/2013 |
| **6.**  Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences) | For patients who have moderate to severe fatigue who are undergoing active anti-cancer therapy, a therapeutic trial of American ginseng could be considered, as long as the patient is not receiving drugs that may interact unfavorably with ginseng, such as anticoagulants |
| **7.** PEPID PCP excerpts[www.pepidonline.com](http://www.pepidonline.com)username: fpinauthorpw: pepidpcp |  |
| **8.** PEPID citation/access data | Author. Title. In: PEPID [database online]. Available at: <http://www.pepidonline.com>. Last updated:. Accessed |
| **9.** PEPID content updating | 1. Do you recommend that PEPID get updated on this topic?[ ]  Yes, there is important evidence or recommendations that are missing[ ]  No, this topic is current, accurate and up to date.If yes, which PEPID Topic, Title(s): 2. Is there an EBM Inquiry (HelpDesk Answers and Clinical Inquiries) as indicated by the EB icon () that should be updated on the basis of the review?[ ]  Yes, there is important evidence or recommendations that are missing[ ]  No, this topic is current, accurate and up to date.If yes, which Evidence Based Inquiry(HelpDesk Answer or Clinical Inquiry), Title(s):  |
| **10.** Other excerpts (USPSTF; other guidelines; etc.) |  |
| **11.** Citations for other excerpts |  |
| **12.**  Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences) |  |
| **SECTION 4: Conclusions** **[to be completed by the Potential PURL Reviewer]** **[to be revised by the Pending PURL Reviewer as needed]** |
| **1.** **Validity:** How well does the study minimize sources of internal bias and maximize internal validity? | Give one number on a scale of 1 to 7(1=extremely well; 4=neutral; 7=extremely poorly)[ ] 1 [x] 2 [x] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **2.** If 4.1 was coded as 4, 5, 6, or 7, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results? |  |
| **3. Relevance:** Are the results of this study generalizable to and relevant to the health care needs of patients cared for by “full scope” family physicians?  | Give one number on a scale of 1 to 7(1=extremely well; 4=neutral; 7=extremely poorly)[ ] 1 [x] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **4.** If 4.3 was coded as 4, 5, 6, or 7,lease provide an explanation. |  |
| **5. Practice changing potential:** If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice? | Give one number on a scale of 1 to 7(1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice)[x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **6.** If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit. | Use of American ginseng root (1 g BID) for cancer-related fatigue. Currently no demonstrated pharmacologic agents to treat CRF. |
| 1. **Applicability to a Family Medical Care Setting:**

Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, educating or counseling a patient; or creating a system for implementing an intervention? | Give one number on a scale of 1 to 7(1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting) [x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **8.** If you coded 4.7 as a 4, 5, 6 or 7, please explain.  |  |
| **9. Immediacy of Implementation:**  Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug or other essentials available on the market? | Give one number on a scale of 1 to 7(1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied) [ ] 1 [x] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **10.** If you coded 4.9 as 4, 5, 6, or 7, please explain why. | Since supplements are often not covered by insurance, some patients may not use due to cost. |
| **11. Clinical meaningful outcomes or patient oriented outcomes:**  Are the outcomes measured in the study clinically meaningful or patient oriented?  | Give one number on a scale of 1 to 7(1=definitely clinically meaningful or patient oriented; 4=uncertain; 7=definitely not clinically meaningful or patient oriented) [ ] 1 [x] 2 [x] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **12.** If you coded 4.11 as a 4, 5, 6, or 7 please explain why. | The results are modest and border on clinically meaningful. Given little other options, a trial of ginseng can be justified. Outcomes are patient oriented. |
| **13.** In your opinion, is this a Pending PURL? Criteria for a Pending PURL:* Valid: Strong internal scientific validity; the findings appears to be true.
* Relevant: Relevant to the practice of family medicine
* Practice changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
* Applicability in medical setting:
* Immediacy of implementation
 | Give one number on a scale of 1 to 7(1=definitely a Pending PURL; 4=uncertain; 7=definitely not a Pending PURL) [x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **14.** Comments on your response in 4.13 | Increasingly, cancer survivorship care is shifting towards primary care providers. Already accepted as a PURL |
| **SECTION 4.1: Diving for PURLs** **[optional for the potential PURL reviewer -if you wish to be the author on the summary]** |
| **1.** Study Summary- Please summarize the study in 5-7 sentences | Patients with cancer diagnoses within the prior 2 years were randomized to receive either standardized American ginseng root capsule or matched placebo. Standardized measures of fatigue were collected at baseline, 4, and 8 weeks. Patients receiving ginseng reported significantly more improvement in fatigue compared to those receiving placebo. The effect was evident only after 8 weeks. Patients who were currently undergoing chemotherapy or radiation appeared to improve more than those who had already completed treatment. There was no difference in adverse events between treatment and placebo groups. |
| 1. Criteria- note yes or no for those which this study meets

 | RELEVENT - yVALID - yCHANGE IN PRACTICE- yMEDICAL CARE SETTING - yIMMEDIATELY APPLICABLE - yCLINICALLY MEANINGFUL - y |
| **3.** Bottom Line- one –two sentences noting the bottom line recommendation  | American Ginseng, 1000 mg twice daily, improves cancer-related fatigue after 8 weeks of treatment. No other treatment has been shown to be effective. |
| **4.** Title Proposal | No longer an untreatable symptom: American Ginseng improves cancer-related fatigue |
| **SECTION 5: Editorial Decisions** **[to be completed by the FPIN PURLs Editor or Deputy Editor]** |
| **1.** FPIN PURLs editorial decision(select one) | [ ] 1 Pending PURL Review—Schedule for Review [ ] 2 Pending PURL—Forward to JFP Editor[ ] 3 Drop |
| 1. Follow up issues for Pending PURL Reviewer

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| **3.** FPIN PURLS Editor making decision  | [ ] 1 Bernard Ewigman[ ] 2 Sarah-Anne Schumann[ ] 3 John Hickner[ ] 4 Kate Rowland |
| **4.** Date of decision |  |
| **5.** Brief summary of decision |  |
| **SECTION 6: Survey Questions for SERMO, PURLs Instant Polls and Other Surveys****[To be completed by the PURLs Survey Coordinator and PURLs Editor]** |
| **1.** Current Practice Question for Surveys |  |
| **2.** Barriers to Implementation Question for Surveys |  |
| **3.** Likelihood of Change Question for Surveys |  |
| **4.** Other Questions for Surveys |  |
| **SECTION 7: Variables for Secondary Database Analyses**  |
| **1.** Population: Age, gender, race, ethnicity |  |
| **2.** Diagnoses |  |
| **3.** Drugs or procedures |  |
| **SECTION 8: Pending PURL Review Assignment****[to be completed by PURLs Project Manager** |
| **1.** Person Assigned for  Pending PURL Review |  |
| **2.** Date Pending PURL Review is due |  |
| **SECTION 9: Pending PURL Review** **[to be completed by the Pending PURL Reviewer]** |
| **1.** Did you address the follow up issues identified at the PURL Jam (Section 5.2). Add comments as needed. | [ ]  Yes[ ]  No[ ]  Not applicable Comments:  |
| **2.** Did you review the Sermo poll & Instant Poll results (if available)? Add comments as needed. | [ ]  Yes[ ]  No[ ]  Not applicable Comments:  |
| **3.** Did you modify Sections 2, 3, or 4? Add comments as needed. | [ ]  Yes[ ]  No[ ]  Not applicable Comments:   |

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| **SECTION 10: PURL Authoring Template** **[to be completed by the assigned PURL Author]** |
| **Author Citation Information** (Name, Degrees, Affiliation) |  |
| **1.** Practice Changer |  |
| **2.** Illustrative Case |  |
| **3.** Background/ Clinical Context/Introduction/Current Practice/ |  |
| **4.** Study Summary |  |
| **5.** What’s New |  |
| **6.** Caveats |  |
| **7.** Challenges to Implementation |  |
| **8.**  Acknowledgment Sentence | The PURLs Surveillance System is supported in part by Grant Number UL1RR024999 from the National Center For Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.**If using UHC data:**We acknowledge Sofia Medvedev of University HealthSystem Consortium (UHC) in Oak Brook, IL for analysis of the National Ambulatory Medical Care Survey data. |
| **9.** References |  |