5 Minute JournalClub

Cooked and Noncooked Diets in Patients with Acute Myeloid Leukemia (AML) Undergoing Remission Induction Therapy

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CME INFORMATION

OVERVIEW OF ACTIVITY

Acute myeloid leukemia (AML) and the myelodysplastic syndromes (MDS) account for approximately 20 percent of all hematologic cancer and related hemopathies diagnosed on an annual basis. Emerging and continuing clinical research has resulted in an increased understanding of the heterogeneous nature of these diseases and in the availability of novel treatment strategies and options. In order to offer optimal patient care — including the option of clinical trial participation — the practicing medical oncologist must be well informed of the rapidly evolving data sets in AML and MDS. To bridge the gap between research and patient care, this CME activity will deliver a serial review of recent key presentations and publications and expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for AML and MDS.

LEARNING OBJECTIVE

- Counsel patients with AML or high-risk MDS who are undergoing remission induction therapy in a protected environment about the evidence for an effect of a neutropenic diet on rate of major infection and probability of survival.

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Oncologists who partake in our **audio series** while they drive in their cars, run on their treadmills or work in their gardens seem to enjoy the often prolonged and Talmudic discussions with master clinical investigators who dissect every corner of medical oncology, but those of you out here in Web World are far more constrained by time, and to that end we offer another iteration of our 5-Minute Journal Club. This latest installment consists of a series of four emails sent at weekly intervals that will highlight approximately 20 recently published journal articles and meeting presentations on MDS/AML deemed by our faculty of Drs Steve Gore and Gail Roboz to be of great relevance to busy physicians in practice. The emails will introduce a specific set of papers and provide links to quickly access slides and faculty comments further explaining the findings from each report.

My favorite out of this first set is the ***JCO* paper by Gardner and colleagues** of a recent trial of 153 patients with newly diagnosed AML receiving induction treatment in a protected environment who were randomly assigned to a cooked (neutropenic) versus an uncooked diet. This fascinating study reveals that the prior belief, upheld by many, that uncooked foods would increase the rates of major infections or death in these patients was unfounded, and while this paper does not bring us any closer to a cure for this dreadful disease, it does provide some solace that those enduring the terrifying experience of induction therapy can enjoy a crispy apple or some grapes while they await the next step in their difficult journey.

Clearly the most practice- and paradigm-changing study profiled herein is the ***Lancet Oncology* paper by Fenaux and colleagues** demonstrating the most important advance in MDS in a long time, specifically that the use of the hypomethylating agent 5-azacitidine was associated with an impressive improvement in overall survival from 15 to 24.5 months in patients with high-risk disease. At a recent CME meeting we hosted in Naples, Florida, Dr Hagop Kantarjian commented that he believes the key to the efficacy of this intriguing agent is the ability to deliver multiple treatment cycles, which was more important than achieving a complete clinical response. He suggested that unlike ARA-C in AML, 5-azacitidine should be continued in MDS even if response is not observed in the first one or two treatment cycles.

Another critical MDS paper included here is a study by Dr Kantarjian examining MD Anderson's rich experience with patients with MDS and chromosome 5 abnormalities. The paper clearly demonstrates the heterogeneity within this uncommon patient subset, in which lenalidomide is often used. Interestingly, in his Naples presentation,

Dr K noted that he thinks this fascinating immunomodulatory agent is also a rational consideration in some patients with MDS *without* chromosome 5 abnormalities, specifically those with low-risk disease and transfusion dependence. In that setting, he believes, lenalidomide results in a transfusion independence rate of about 25 percent.

Finally, we have **an AML paper** that somehow escaped Dan Haller's *JCO* clutch and slipped into the *New England Journal* — a study demonstrating more CRs and better survival in patients receiving 90-mg/m^2 of daunorubicin than those receiving 45-mg/m^2. Dr Roboz questions the relevance of these findings because of the 45-mg/m^2 control arm, as she believes most physicians are using the 60-mg/m^2 dose.

Stay tuned for our next journal club, in which we review yet another paper by the prolific Dr Kantarjian proposing a new prognostic model for MDS, an MDS study evaluating the impact of pretransplant 5-azacitidine on the risk of post-transplant relapse, a study of decitabine in older patients with MDS and another paper on 5-azacitidine in MDS evaluating three different doses/schedules.

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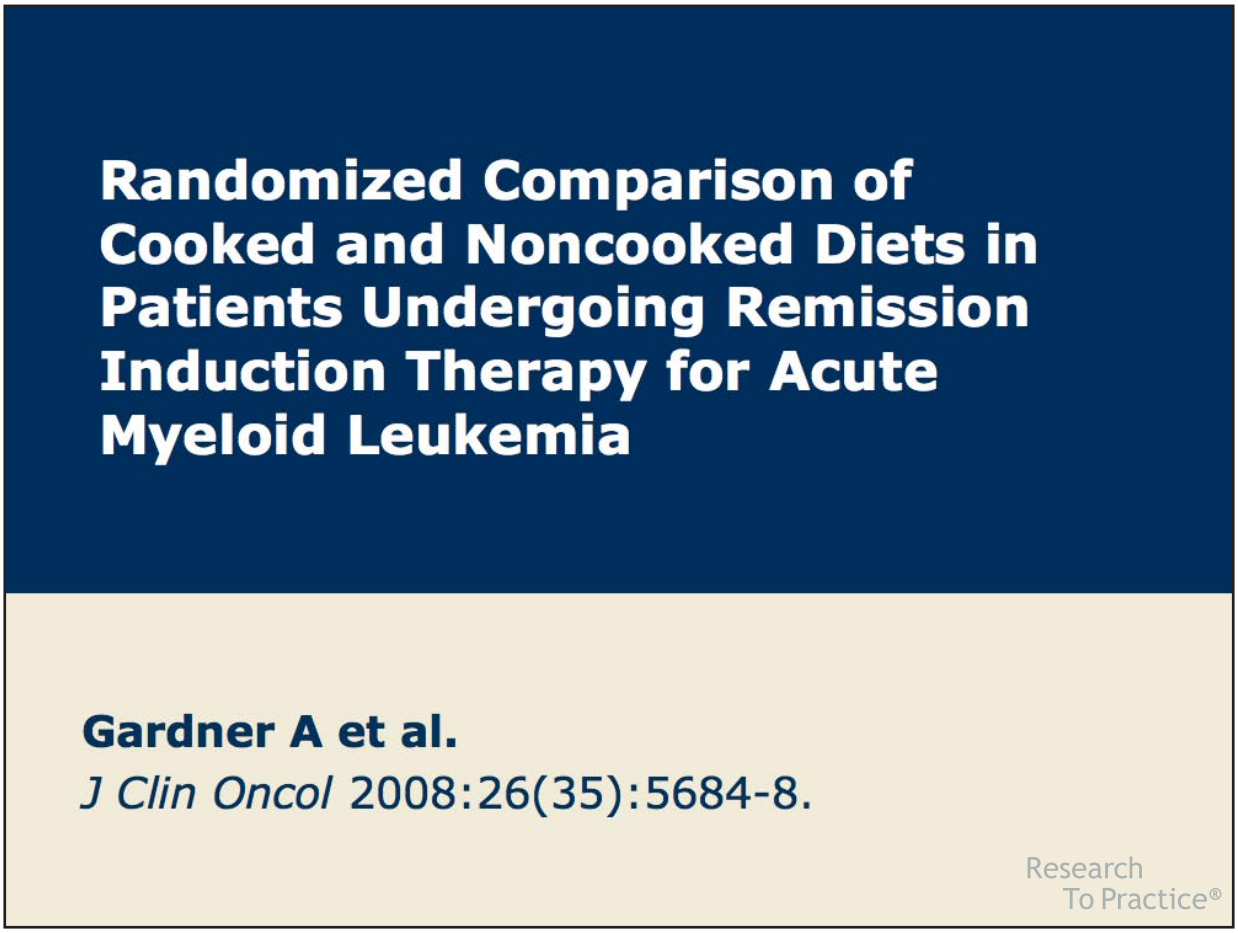
Cooked and Noncooked Diets in Patients with Acute Myeloid Leukemia (AML) Undergoing Remission Induction Therapy

Presentation discussed in this issue:

Gardner A et al. **Randomized comparison of cooked and noncooked diets in patients undergoing remission induction therapy for acute myeloid leukemia.** *J Clin Oncol* 2008;26(35):5684-8. **Abstract**

Slides from the journal article and transcribed comments from a recent interview with Steven D Gore, MD (10/8/09) below



Introduction

- Majority of neutropenic diets restrict consumption of raw vegetables, fruits and juices due to their possible contamination with Gram-negative bacilli that may lead to life-threatening infections and pneumonia.
- Small trials in children (n = 19) or in adults (n = 20) evaluating neutropenic diets did not provide evidence to support their routine use (*J Pediatr Hematol Oncol* 2006;28:126; *Ann Oncol* 2007;18:1080).
- **Current study objectives (N = 153):**
  - Patients with untreated acute myeloid leukemia (AML) or high-risk myelodysplastic syndrome (MDS) who were about to receive remission induction therapy in a protected environment (PE) were randomized to a diet containing raw fruits and vegetables or a diet containing fruits and vegetables only if cooked.
  - Primary outcomes measured were the rate of major infection and the probability of death

Source: Gardner A et al. *J Clin Oncol* 2008;26(35):5684-8.

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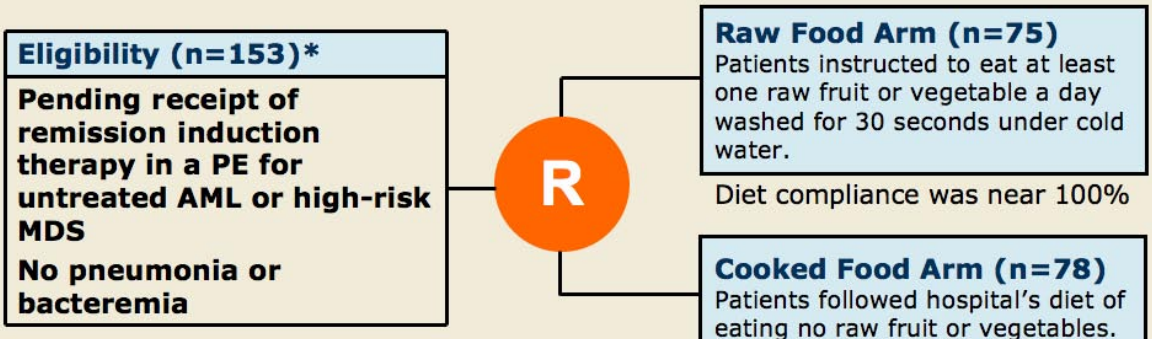
Single-Site, Randomized Comparison of Cooked versus Noncooked Diets in Patients with AML



**53 patients of 206 eligible refused randomization (non-randomized group) and followed hospital's diet (cooked diet)*

All patients received antimicrobial and antifungal prophylaxis. Patients in the two randomized groups were similar with respect to age, early risk of mortality (ERM), chemotherapy received and days at risk.

Source: Gardner A et al. *J Clin Oncol* 2008;26(35):5684-8.

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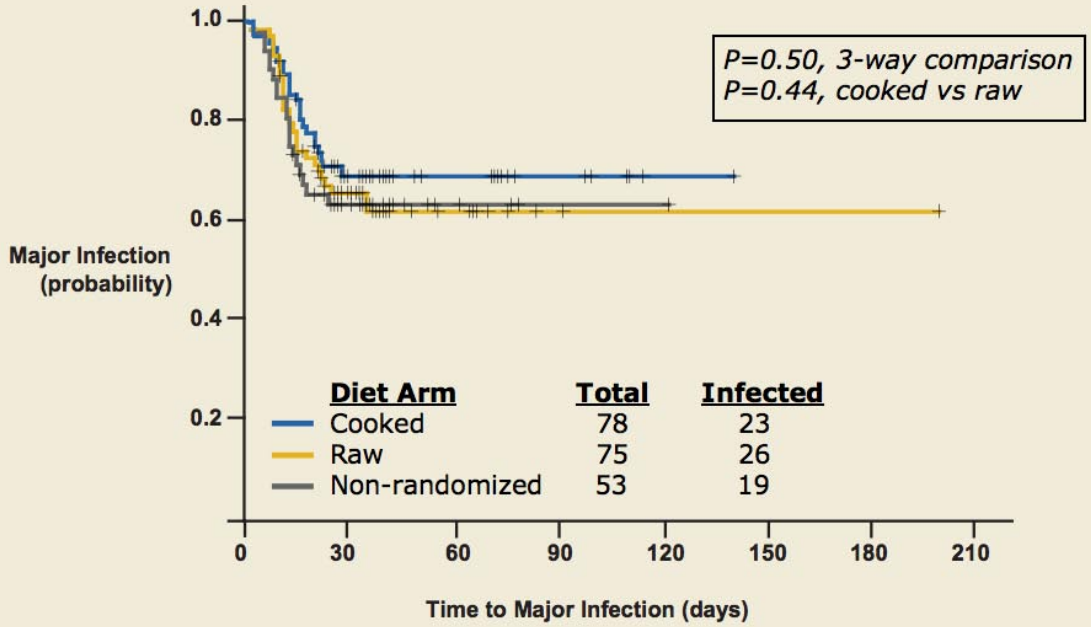
Incidence of Infection or Fever of Unknown Origin (FUO)

Infection and FUO	Raw Food (n=75)	Cooked Food (n=78)	*P*-value
Patients with any major infection[1]	35%	29%	0.60
Pneumonia	**5%**	**15%**	**0.06**
Bacteremia or fungemia	**23%**	**9%**	**0.03**
Pneumonia + bacteremia or fungemia	7%	5%	0.74
Patients with any minor infection	5%	6%	0.99
Patients with FUO	36%	51%	0.07
Patients with major or minor infection	40%	36%	0.62
Patients with infection or FUO[2]	76%	87%	0.09

[1,2]Rate of major infection in the non-randomized group was 36% and rate of infection or FUO was 85%.

Source: Gardner A et al. *J Clin Oncol* 2008;26(35):5684-8.

Probability of Major Infection of Patients In Different Dietary Study Arms



Source: Reprinted with permission. Gardner A et al. *J Clin Oncol* 2008;26(35):5684-8.

Selected Organisms Isolated from Patients with Major Infections

Organism	Number of Patients		
	Raw Food	Cooked Food	Non-randomized
Patients with pneumonia (n=28)			
Aspergillis	—	1	—
Unknown	4	11	12
Patients with bacteremia/fungemia ± Pneumonia (n=41)			
E. coli	3	2	—
Enterococcus	5*	2	1
Enterobacter	1	—	1
Coagulase-neg. Staphylococcus	3	1	1
α-Hemolytic Streptococcus	5	1	—
Fusarium	1*	—	—

**One patient had Enterococcus and Fusarium.*

Source: Gardner A et al. *J Clin Oncol* 2008;26(35):5684-8.

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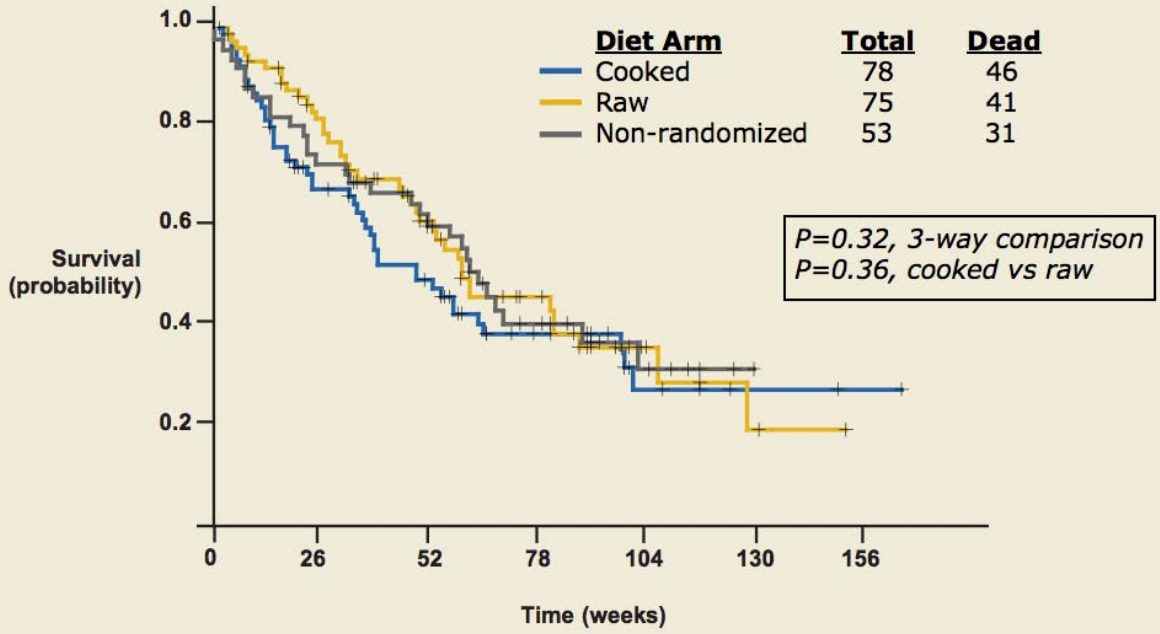
Survival Probability of Patients in Different Dietary Study Arms



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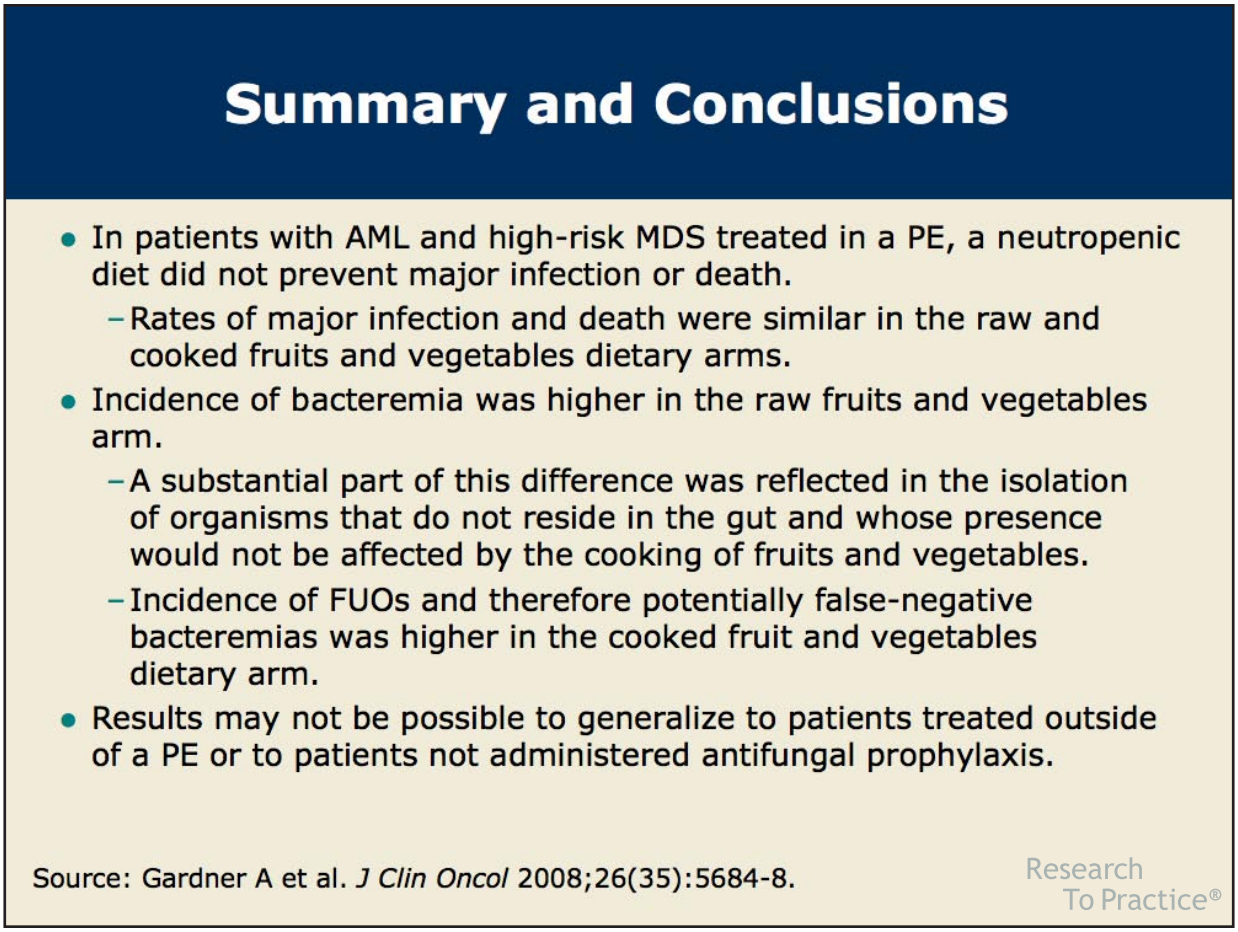

STEVEN D GORE, MD: A whole mythology has existed for many moons now that patients with AML and neutropenia in a protected environment should not eat raw foods or vegetables, but it is based on someone's hunch 30-some years ago. This limits patients in terms of what they can eat, and the question arises whether that inconvenience is worth imposing on the patient.

I think this is a great idea for a randomized study. They found that 35 percent of patients in the study arm allowed to consume raw fruits and vegetables developed major infections versus 29 percent of patients in the study arm that only consumed fruits and vegetables in cooked form. This difference was not statistically significant. This is great news for patients because they should be able to eat whatever they want. This has been our practice at Hopkins. It may seem like a small issue, but when you are a patient in the hospital for 35 days and you like fruit, it is nice to be able to eat it.

Dr Gore is Professor of Oncology at Johns Hopkins University in Baltimore, Maryland.