

ESMO SYMPOSIUM ON CANCER & NUTRITION

Cancer Chemotherapy:
With or Without Food?

Aminah Jatoi, M.D.

Mayo Clinic

Rochester, Minnesota USA

QUESTIONS

- Does oral chemotherapy have any adverse effects just because it's oral?
- What should we tell patients about food intake prior to taking chemotherapy?
- What about food prior to intravenous chemotherapy?

Currently 10% of cancer
chemotherapy drugs are oral.

By 2013, it'll be 25%.

NCCN Report, 2008

Advantages of Oral Chemotherapy

- No need for IV access
- More time at home
- Greater sense of patient empowerment

DATE	GENERIC NAME	BRAND NAME	FDA INDICATION
March 2005	Temozolomide	Temodar® (Schering Corporation)	GBM
June 2005	Capecitabine	Xeloda® (Roche Laboratories Inc.)	Adjuvant Dukes C colon cancer
December 2005	Sorafenib	Nexavar® (Bayer Pharmaceuticals)	Renal cell cancer
December 2005	Lenalidomide	Revlimid® (Celgene Corporation)	MDS
January 2006	Sunitinib	Sutent® (Pfizer Inc.)	GIST or failure of Gleevec® renal cell cancer
May 2006	Thalidomide	Thalomid® (Celgene Corporation)	In combination with decadron for newly diagnosed multiple myeloma
June 2006	Dasatinib	Sprycel™ (Bristol-Myers Squibb)	CML resistant
June 2006	Lenalidomide	Revlimid® (Celgene Corporation)	With decadron for patients with multiple myeloma who have received one regimen
September 2006	Imatinib mesylate	Gleevec® (Novartis Pharmaceuticals Corporation)	Pediatric Ph+CML
June 2006	Volinostat	Zolinza® (Merck & Co., Inc.)	Cutaneous T-cell lymphoma
March 2007	Lapatinib	Tykerb® (GlaxoSmithKline)	In combination with Xeloda in patients with breast cancer who have received a taxane, anthracycline, and trastuzumab

Winkeljohn D, Clinical Journal of Oncology Nursing, 2007.

And the “Older Agents:”

- Etoposide
- Cyclophosphamide
- Idarubicin
- CCNU
- Chlorambucil
- Hormonal agents

Does oral chemotherapy have any adverse effects just because it's oral?

NEXT TO NO DATA:

- Does the bitter taste of oral chemotherapy effect adherence?
- Are there psychological effects from asking patients to fast before oral chemotherapy?

Anecdotes from the pediatric
literature:

The bitterness of prednisone
results in poor compliance
during maintenance cancer
therapy.

Another anecdote:

With oral or intravenous chemotherapy, eating one's favorite foods can diminish the pleasure of eating such foods thereafter.

QUESTIONS

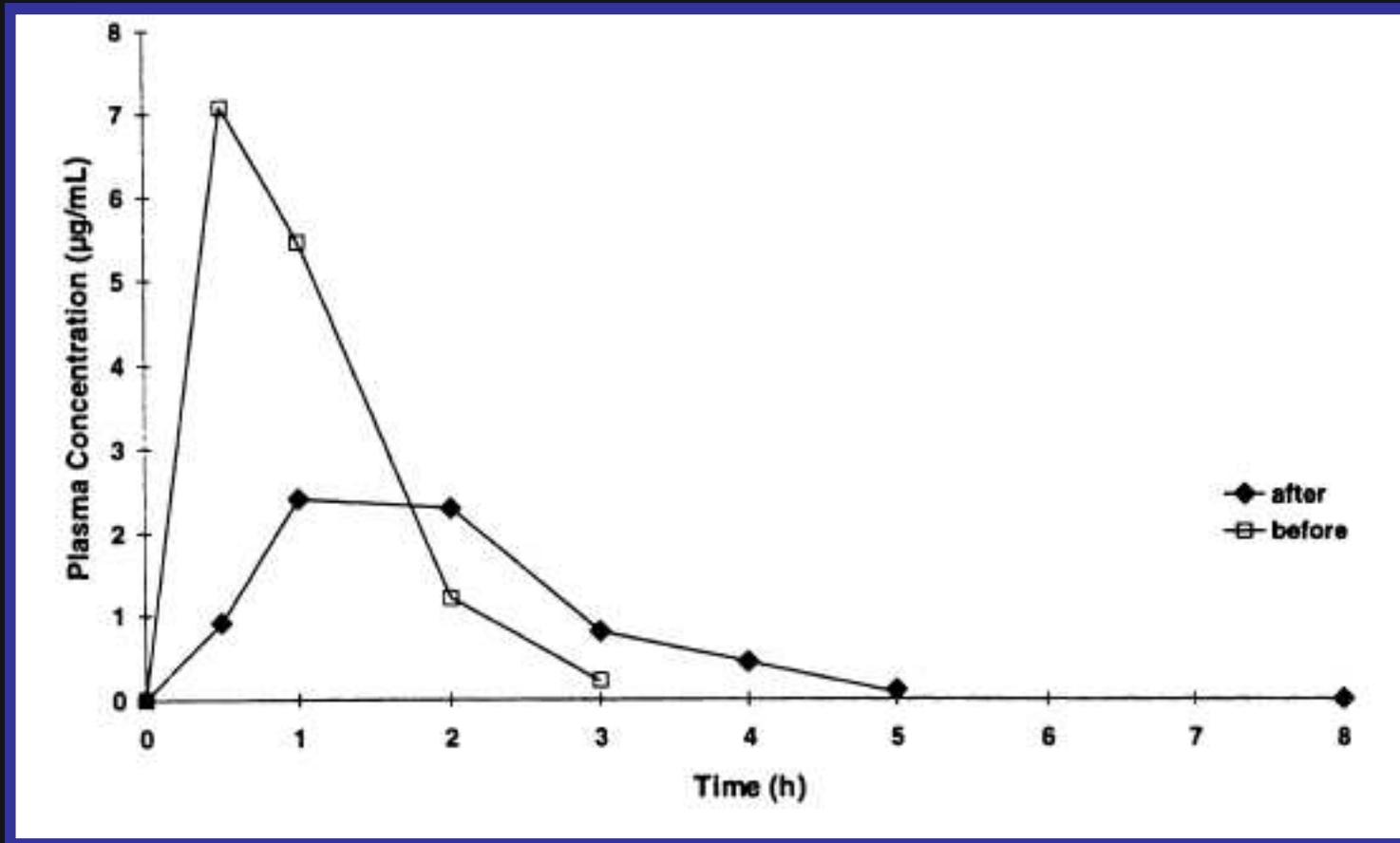
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Food may...

- delay oral chemotherapy absorption due to gastric emptying
- decrease chemotherapy absorption due to drug instability in gastric fluids or chemical binding
- increase absorption by increasing drug solubility, decreasing the 1st pass effect, increasing the permeability of the epithelial membranes

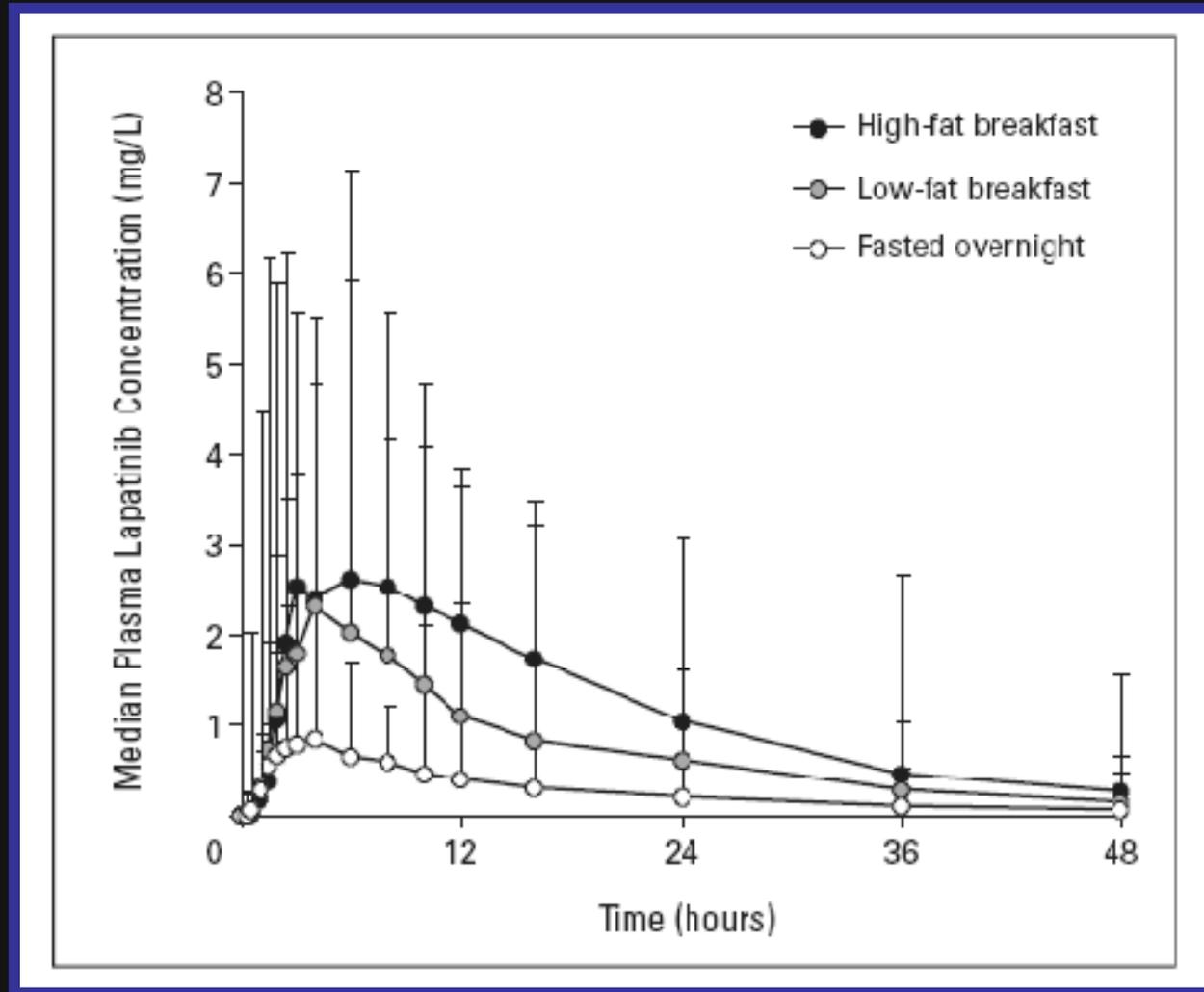
1) FASTING INCREASED THE RATE AND EXTENT OF CAPECITABINE ABORPTION

2) FOOD INTAKE 30' PRIOR STABILIZES SUCH EFFECTS



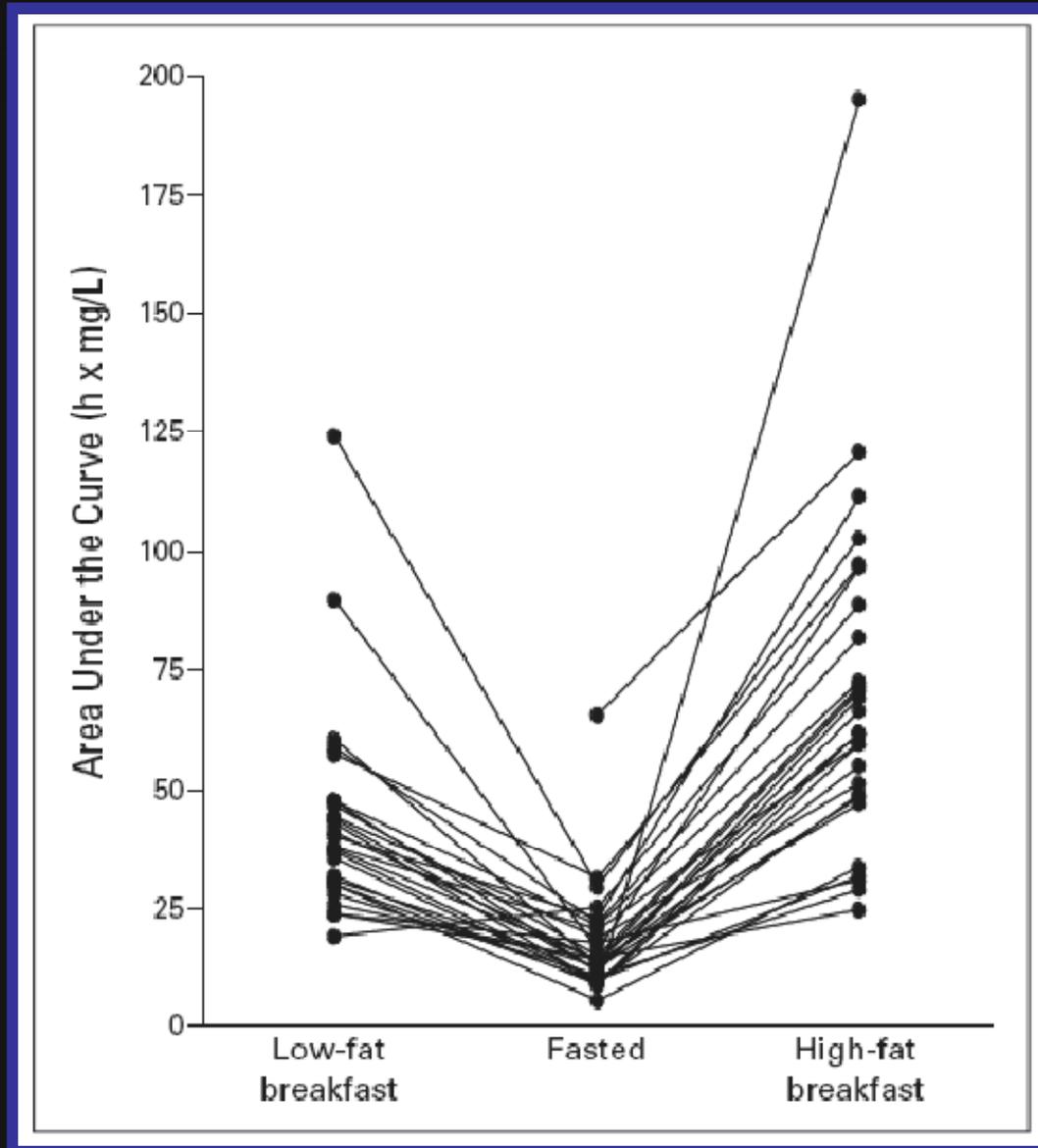
Reigner et al. Clin Cancer Res, 1998.

FOOD AFFECTS LAPATINIB ABSORPTION



Koch, et al. JCO, 2009.

FAT INTAKE AND LAPATINIB



BOTTOM LINE:

Follow the directions on the drug package insert... and provide this information to patients.

Does food type influence
absorption?



Grapefruit juice, a potent inhibitor of CYP3A4:

- Methadone
- Oxycodone
- Vinblastine

QUESTIONS

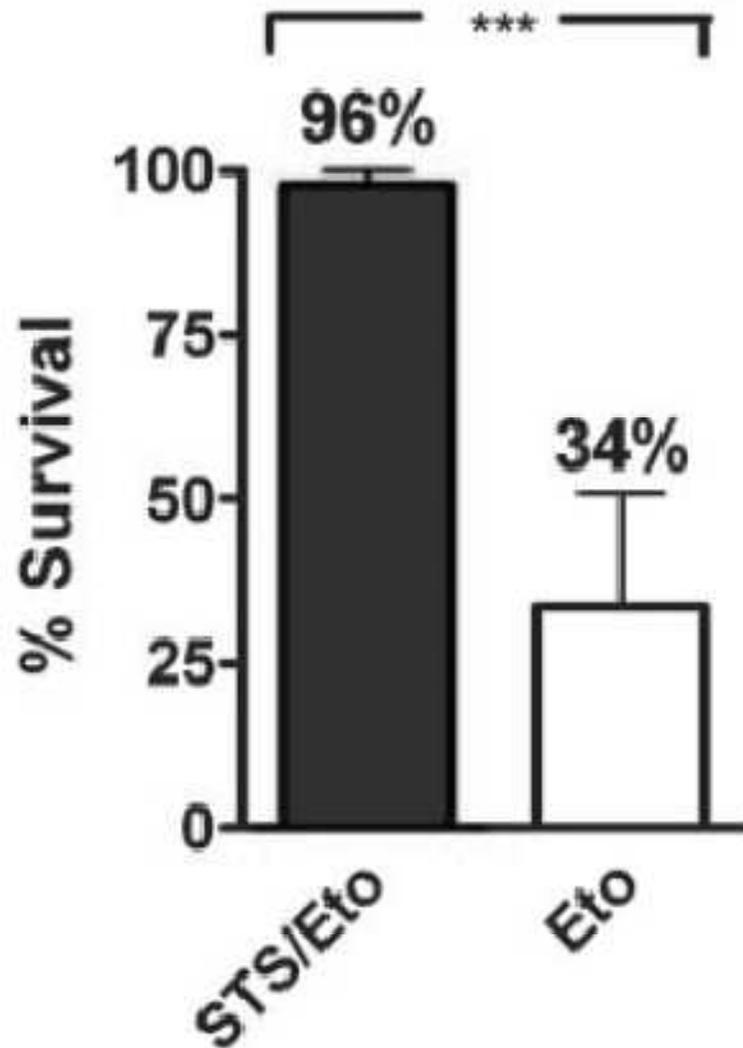
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Hypothesis:

Fasting slows metabolism in normal cells and therefore leads to less chemotherapy-induced toxicity.

Because cancer cells, are unregulated, they continue to be vulnerable to chemotherapy even during fasting.

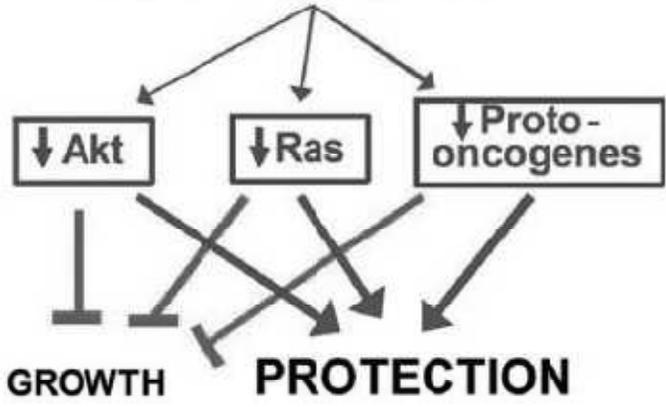
Starvation Prior to Chemotherapy Resulted in Improved Survival:



Raffaghello L, et al. PNAS, 2008

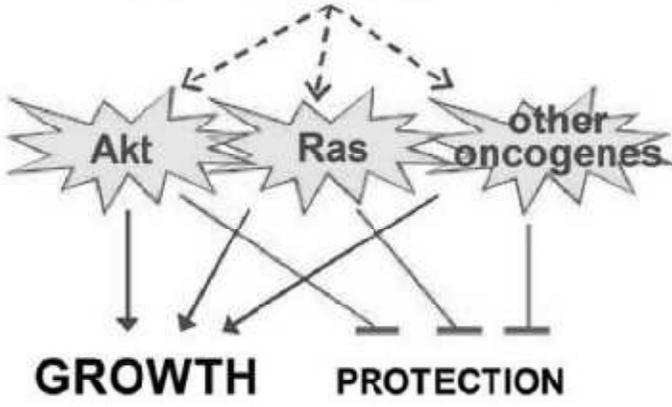
Normal Cells

Short-Term Starvation



Tumor Cells

Short-Term Starvation



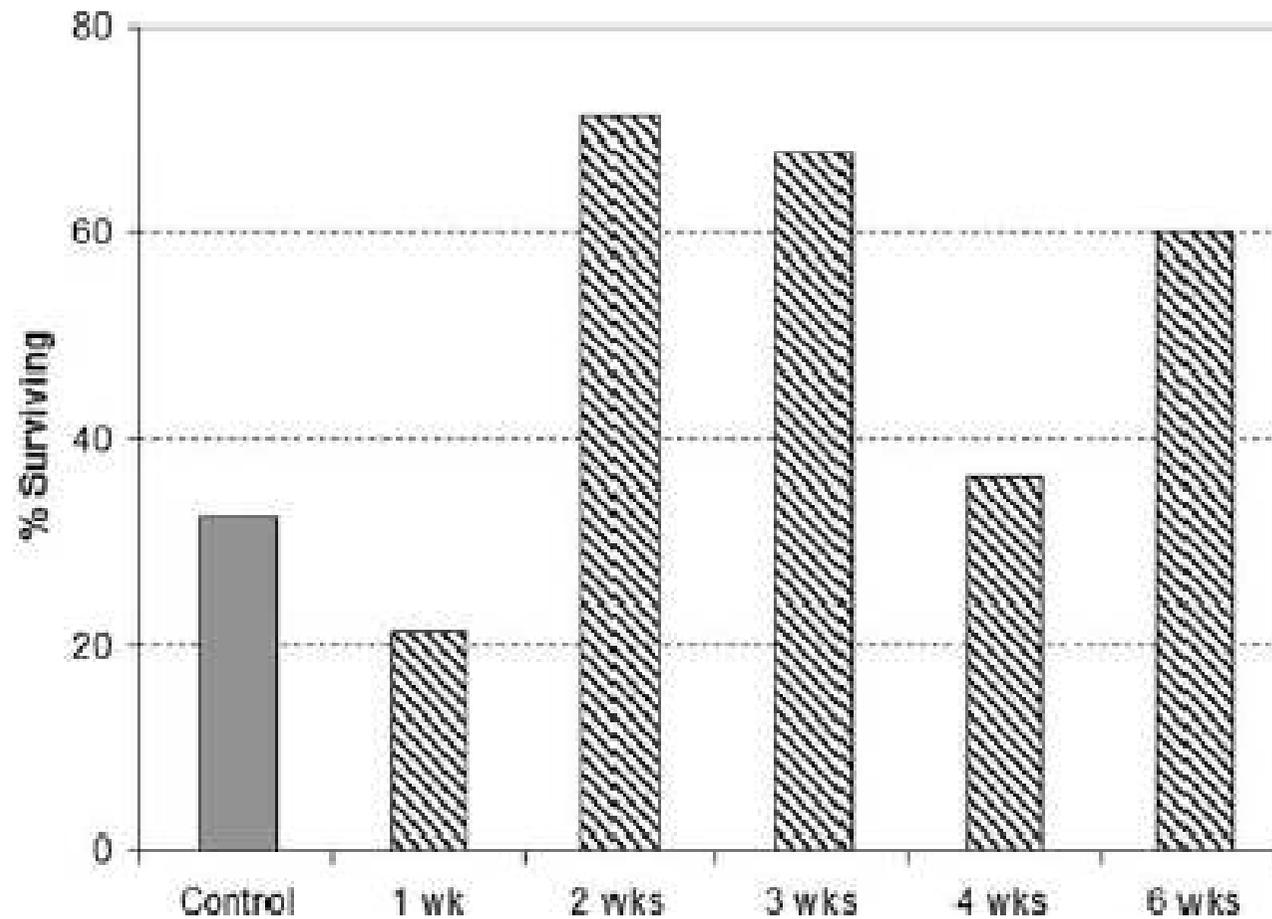
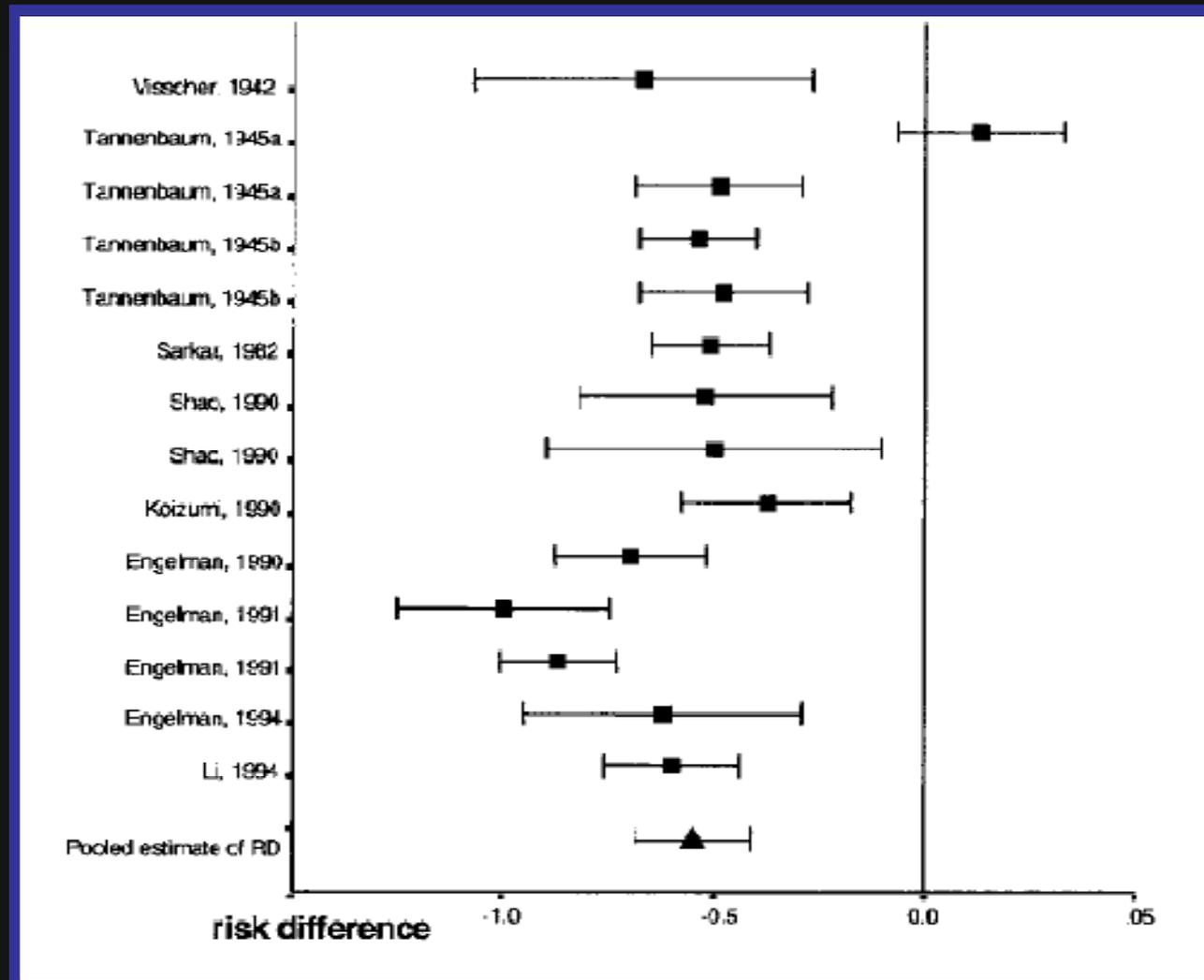


Fig. 1. Composite average survival after whole body radiation of three different mouse strains following intervals of 1–6 weeks of alternate day feeding (ADF).

Johnson, et al. Medical Hypotheses, 2009

CALORIC RESTRICTION DECREASES CANCER INCIDENCE



Dirx et al. Int J Cancer, 2003

Should we recommend that patients fast
prior to chemotherapy?

No.

- “Would I be enthusiastic about enrolling my patients on a trial where they’re asked not to eat for 2 1/2 days? No.”

– Leonard Saltz, M.D.

- “... it really goes against a lot of the thoughts that people have, that you need to eat to feel better.”

– Alan Sandler, M.D.

Couzin J. Science, 2008

Ongoing Clinical Trials

- NCT00757094: King Fahad Medical City; tests the safety of fasting before chemotherapy during Ramadan
- University of Southern California: trial in development; funded by the V Foundation

SUMMARY POINTS:

- We need to learn more about oral chemotherapy, quality of life, and compliance.
- We need to learn more about interactions between food and oral chemotherapy.
- Follow the directions on the package insert when prescribing oral chemotherapy.
- Don't tell cancer patients to fast prior to intravenous chemotherapy until we learn more.