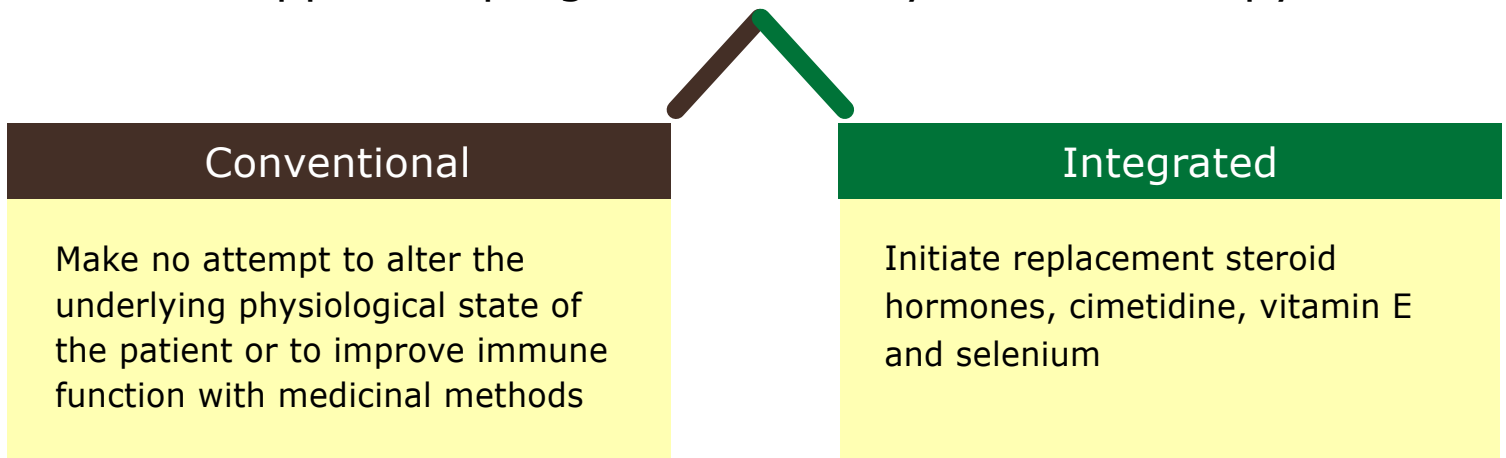


Critical Decisions in a Successful Immunotherapeutic Pathway

Decision Forks for Earl Daniels: A Comparison of Conventional Versus Integrative Management Philosophies

Fork 1

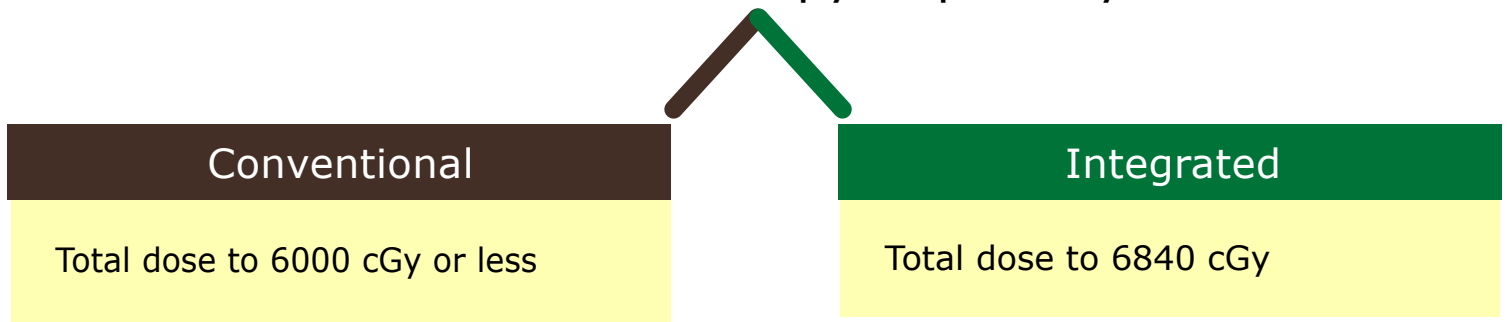
Supportive program – first day of radiotherapy



Result: Less mucous membrane toxicity was induced, facilitating delivery of a higher total dose at completion. Medicines to some degree protected against immunosuppression from chemotherapy.

Fork 2

Final dose of radiotherapy to primary tumor



Result: Based on radiobiological log killing concepts, clonagens (surviving cancer cells capable of repeated division) in treatment volume reduced by an additional 99%.

Fork 3

Decision to participate in the integrative cancer treatment model; management at chemotherapy termination



Conventional

Common decision would have been "watchful waiting" = no active intervention.

Integrated

Add interleukin-2 belly plaque (see photo) to previous oral agent immune regimen, realizing cessation of cytotoxic chemotherapy could permit restoration of immune cancer defenses if intense immune stimulation was initiated and sustained. At this point, it was essential that a physician knowledgeable in immune restoration be in control of treatment management. A decision to replace cytotoxic chemotherapy with immunotherapy should always be a patient decision.

Result: Less mucous membrane toxicity was induced, facilitating delivery of a higher total dose at completion. Medicines to some degree protected against immunosuppression from chemotherapy.

Fork 4

Dosage of radiotherapy for brain metastases



Conventional

Commonly employed dose is 3000 cGy in 10 treatments over 2 weeks.

Integrated

Recognize the possibility that the brain metastases occurred because the cancer has escaped chemotherapy during the cytotoxic initial management due to the blood brain barrier. Therefore, there was not sufficient reason to presume this sanctuary relapse was indicative of hopeless systemic spread. Radiotherapy was given to adequate dose approaching tumorocidal for 2 cm masses, adequate to control some brain metastases. Dose given was 4000 cGy in 4 weeks.

Result: Much more thorough eradication of brain cancer cells by at least 99% and superior preservation of cognitive function due to smaller daily dose of radiotherapy.

Fork 5

Whether or not to accept systemic management
at the end of brain radiotherapy



Conventional

Start more chemotherapy on the presumption that the brain metastases indicated impending systemic relapse.

Integrated

Decide that sanctuary intracranial relapse did not conclusively indicate other distant sites, and further chemotherapy is not recommended as immunotherapy is compatible with sustained high quality remissions not possible with chemotherapy. Immunotherapeutic program was sustained with no interruption.

Result: NK elevation and hyperimmune state not damaged.

Fork 6

What is our next step?

PET scan shows interval development of adrenal metastasis.
CEA evidencing progressive growth of cancer (serologic failure).
CT of abdomen confirms large belly plaque.



Conventional

Conclude that adrenal metastasis is proof of systemic failure and advise further cytotoxic chemotherapy, OR give up and abandon all treatment.

Integrated

Interpret adrenal recurrence as another sanctuary relapse phenomenon, typical of adenocarcinoma of the lung, not necessarily a fundamental failure of immunotherapeutic strategy. Brain and adrenal metastases are characteristic "fertile soil" recurrence patterns in lung adenocarcinoma, but likely develop by completely different mechanisms. Treat adrenal sanctuary site with sterilizing dose of radiotherapy after Iressa sensitization.

Result: Local control in the adrenal and subsequent drop in CEA to stabilize in normal range. As of January 2005, there has been systemic serologic control and no clinical evidence of systemic progression. Quality of life is excellent.

Fork 7

Patient is NED (no evidence of disease) status based on Irredia sensitized radiotherapy to only PET scan positive site. Mr. Daniels asks, "Is it safe to stop Iressa?"

Iressa is expensive, causes skin rash and some diarrhea in many patients, and may have long term deleterious effects.



Conventional

Tumor recurred after previous normalization. It is disseminated non-small cell lung cancer and will surely recur with time. Some form of persistent chemotherapy for systemic control is indicated.

Integrated

The original CEA drop (see graph) after combined concurrent radiotherapy and chemotherapy was a strictly cytotoxic driven drop, undoubtedly accompanied by significant hematopoietic depression, low blood white counts (lymphopenia), and incapacity of the lymphocyte driven immune system to combat residual cancer. The second CEA drop after adrenal radiotherapy occurred in the context of documented marked elevation of peripheral blood NK cells. Thus, systemic status was qualitatively different at the second occasion. It was possible that body burden had fallen to the threshold where natural immunity, enhanced by integrated approach (cimetidine, miatake fraction D, selenium, etc.) could affect final extermination of microscopic clonagens. It was, therefore, reasonable to initiate a CEA monitored clinical trial off Iressa.

Result: CEA has remained in normal range off IL-2 and Iressa. Patient is active and productive. He and his wife are happy (see video). An anomalous protracted survival is in place maintained because of either (1) residual tumor is in growth arrest or because (2) all tumor has been eradicated. Patient with extensive disease is now positioned to become a long term survivor.

Overall result of decisions at critical decision forks

Sustained high quality of life, no evidence of disease (NED) survival. Good cognitive function, physical strength, mood, and immune resistance are preserved or restored in spite of previous advanced cancer and extensive chemotherapy and brain radiotherapy.